

TITLE OF THE INVENTION

CONE SNAIL PEPTIDES

CROSS-REFERENCE TO RELATED APPLICATIONS

5 [0001] The present application is related to and claims priority under 35 USC §119(e) to U.S. provisional patent application Serial No. 60/267,408 filed 9 February 2001, incorporated herein by reference.

[0002] This invention was made with Government support under Grant No. PO1 GM48677 awarded by the National Institute of General Medical Sciences, National Institutes of Health, Bethesda, Maryland. The United States Government has certain rights in the invention.

BACKGROUND OF THE INVENTION

[0003] The present invention is directed to conotoxin peptides, derivatives or pharmaceutically acceptable salts thereof. The present invention is further directed to the use of this peptide, derivatives thereof and pharmaceutically acceptable salts thereof for the treatment of disorders associated with voltage-gated ion channels, ligand-gated ion channels and/or receptors. The invention is further directed to nucleic acid sequences encoding the conotoxin peptides and encoding propeptides, as well as the propeptides.

20 [0004] The publications and other materials used herein to illuminate the background of the invention, and in particular, cases to provide additional details respecting the practice, are incorporated by reference, and for convenience are referenced in the following text by author and date and are listed alphabetically by author in the appended bibliography.

[0005] *Conus* is a genus of predatory marine gastropods (snails) which envenomate their
25 prey. Venomous cone snails use a highly developed projectile apparatus to deliver their cocktail of toxic conotoxins into their prey. In fish-eating species such as *Conus magus* the cone detects the presence of the fish using chemosensors in its siphon and when close enough extends its proboscis and fires a hollow harpoon-like tooth containing venom into the fish. This immobilizes the fish and enables the cone snail to wind it into its mouth via an attached filament.
30 For general information on *Conus* and their venom see the website address <http://grimwade.biochem.unimelb.edu.au/cone/referenc.html>. Prey capture is accomplished through a sophisticated arsenal of peptides which target specific ion channel and receptor subtypes. Each *Conus* species venom appears to contain a unique set of 50-200 peptides. The

composition of the venom differs greatly between species and between individual snails within each species, each optimally evolved to paralyse its prey. The active components of the venom are small peptide toxins, typically 12-30 amino acid residues in length and are typically highly constrained peptides due to their high density of disulphide bonds.

5 [0006] The venoms consist of a large number of different peptide components that when separated exhibit a range of biological activities: when injected into mice they elicit a range of physiological responses from shaking to depression. The paralytic components of the venom that have been the focus of recent investigation are the α -, ω - and μ -conotoxins. All of these conotoxins act by preventing neuronal communication, but each targets a different aspect of the process to achieve this. The α -conotoxins target nicotinic ligand gated channels, the μ -conotoxins target the voltage-gated sodium channels and the ω -conotoxins target the voltage-gated calcium channels (Olivera et al., 1985; Olivera et al., 1990). For example a linkage has been established between α -, αA - & ϕ -conotoxins and the nicotinic ligand-gated ion channel; ω -conotoxins and the voltage-gated calcium channel; μ -conotoxins and the voltage-gated sodium channel; δ -conotoxins and the voltage-gated sodium channel; κ -conotoxins and the voltage-gated potassium channel; conantokins and the ligand-gated glutamate (NMDA) channel.

20 [0007] However, the structure and function of only a small minority of these peptides have been determined to date. For peptides where function has been determined, three classes of targets have been elucidated: voltage-gated ion channels; ligand-gated ion channels, and G-protein-linked receptors.

[0008] *Conus* peptides which target voltage-gated ion channels include those that delay the inactivation of sodium channels, as well as blockers specific for sodium channels, calcium channels and potassium channels. Peptides that target ligand-gated ion channels include antagonists of NMDA and serotonin receptors, as well as competitive and noncompetitive
25 nicotinic receptor antagonists. Peptides which act on G-protein receptors include neurotensin and vasopressin receptor agonists. The unprecedented pharmaceutical selectivity of conotoxins is at least in part defined by a specific disulfide bond frameworks combined with hypervariable amino acids within disulfide loops (for a review see McIntosh et al., 1998).

30 [0009] There are drugs used in the treatment of pain, which are known in the literature and to the skilled artisan. See, for example, Merck Manual, 16th Ed. (1992). However, there is a demand for more active analgesic agents with diminished side effects and toxicity and which are non-addictive. The ideal analgesic would reduce the awareness of pain, produce analgesia over a

wide range of pain types, act satisfactorily whether given orally or parenterally, produce minimal or no side effects, be free from tendency to produce tolerance and drug dependence.

[0010] Due to the high potency and exquisite selectivity of the conopeptides, several are in various stages of clinical development for treatment of human disorders. For example, two *Conus* peptides are being developed for the treatment of pain. The most advanced is ω -conotoxin MVIIA (ziconotide), an N-type calcium channel blocker (see Heading, C., 1999; U.S. Patent No. 5,859,186). ω -Conotoxin MVIIA, isolated from *Conus magus*, is approximately 1000 times more potent than morphine, yet does not produce the tolerance or addictive properties of opiates. ω -Conotoxin MVIIA has completed Phase III (final stages) of human clinical trials and has been approved as a therapeutic agent. ω -Conotoxin MVIIA is introduced into human patients by means of an implantable, programmable pump with a catheter threaded into the intrathecal space. Preclinical testing for use in post-surgical pain is being carried out on another *Conus* peptide, contulakin-G, isolated from *Conus geographus* (Craig et al. 1999). Contulakin-G is a 16 amino acid O-linked glycopeptide whose C-terminus resembles neurotensin. It is an agonist of neurotensin receptors, but appears significantly more potent than neurotensin in inhibiting pain in *in vivo* assays.

[0011] In view of a large number of biologically active substances in *Conus* species it is desirable to further characterize them and to identify peptides capable of treating disorders voltage-gated ion channels, ligand-gated ion channels and/or receptors. Surprisingly, and in accordance with this invention, Applicants have discovered novel conotoxins that can be useful for the treatment of disorders involving voltage-gated ion channels, ligand-gated ion channels and/or receptors and could address a long felt need for a safe and effective treatment.

SUMMARY OF THE INVENTION

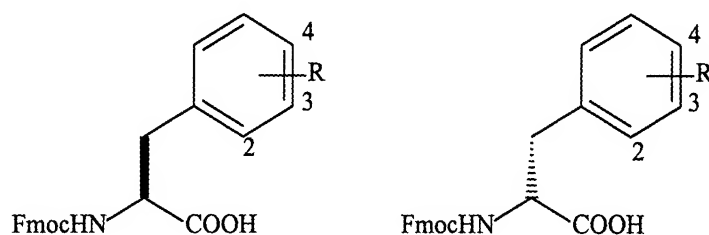
[0012] The present invention is directed to conotoxin peptides, derivatives or pharmaceutically acceptable salts thereof. The present invention is further directed to the use of this peptide, derivatives thereof and pharmaceutically acceptable salts thereof for the treatment of disorders associated with voltage-gated ion channels, ligand-gated ion channels and/or receptors. The invention is further directed to nucleic acid sequences encoding the conotoxin peptides and encoding propeptides, as well as the propeptides.

[0013] More specifically, the present invention is directed to conotoxin peptides, having the amino acid sequences set forth in Tables 1-14 below.

[0014] The present invention is also directed to derivatives or pharmaceutically acceptable salts of the conotoxin peptides or the derivatives. Examples of derivatives include peptides in which the Arg residues may be substituted by Lys, ornithine, homoargine, nor-Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any synthetic basic amino acid; the Lys residues may be substituted by Arg, ornithine, homoargine, nor-Lys, or any synthetic basic amino acid; the Tyr residues may be substituted with meta-Tyr, ortho-Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any synthetic hydroxy containing amino acid; the Ser residues may be substituted with Thr or any synthetic hydroxylated amino acid; the Thr residues may be substituted with Ser or any synthetic hydroxylated amino acid; the Phe residues may be substituted with any synthetic aromatic amino acid; the Trp residues may be substituted with Trp (D), neo-Trp, halo-Trp (D or L) or any aromatic synthetic amino acid; and the Asn, Ser, Thr or Hyp residues may be glycosylated. The halogen may be iodo, chloro, fluoro or bromo; preferably iodo for halogen substituted-Tyr and bromo for halogen-substituted Trp. The Tyr residues may also be substituted with the 3-hydroxyl or 2-hydroxyl isomers (meta-Tyr or ortho-Tyr, respectively) and corresponding O-sulpho- and O-phospho-derivatives. The acidic amino acid residues may be substituted with any synthetic acidic amino acid, e.g., tetrazolyl derivatives of Gly and Ala. The aliphatic amino acids may be substituted by synthetic derivatives bearing non-natural aliphatic branched or linear side chains C_nH_{2n+2} up to and including $n=8$. The Leu residues may be substituted with Leu (D). The Glu residues may be substituted with Glu. The Gla residues may be substituted with Glu. The N-terminal Gln residues may be substituted with pyroGlu. The Met residues may be substituted with norleucine (Nle). The Cys residues may be in D or L configuration and may optionally be substituted with homocysteine (D or L).

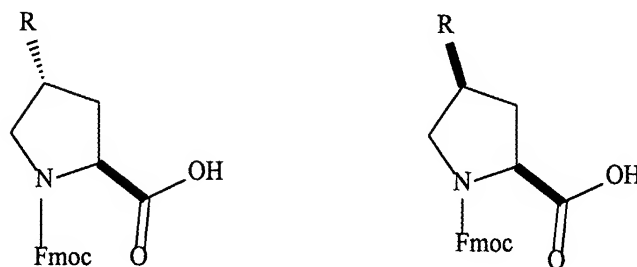
[0015] Examples of synthetic aromatic amino acid include, but are not limited to, nitro-Phe, 4-substituted-Phe wherein the substituent is C_1 - C_3 alkyl, carboxyl, hydroxymethyl, sulphomethyl, halo, phenyl, -CHO, -CN, -SO₃H and -NHAc. Examples of synthetic hydroxy containing amino acid, include, but are not limited to, such as 4-hydroxymethyl-Phe, 4-hydroxyphenyl-Gly, 2,6-dimethyl-Tyr and 5-amino-Tyr. Examples of synthetic basic amino acids include, but are not limited to, N-1-(2-pyrazolinyl)-Arg, 2-(4-piperinyl)-Gly, 2-(4-piperinyl)-Ala, 2-[3-(2S)pyrrolinyl]-Gly and 2-[3-(2S)pyrrolinyl]-Ala. These and other synthetic basic amino acids, synthetic hydroxy containing amino acids or synthetic aromatic amino acids are described in Building Block Index, Version 3.0 (1999 Catalog, pages 4-47 for

hydroxy containing amino acids and aromatic amino acids and pages 66-87 for basic amino acids; see also <http://www.amino-acids.com>), incorporated herein by reference, by and available from RSP Amino Acid Analogues, Inc., Worcester, MA. The residues containing protecting groups are deprotected using conventional techniques. Examples of synthetic acid amino acids include those derivatives bearing acidic functionality, including carboxyl, phosphate, sulfonate and synthetic tetrazolyl derivatives such as described by Ornstein et al. (1993) and in U.S. Patent No. 5,331,001, each incorporated herein by reference, and such as shown in the following schemes 1-3.



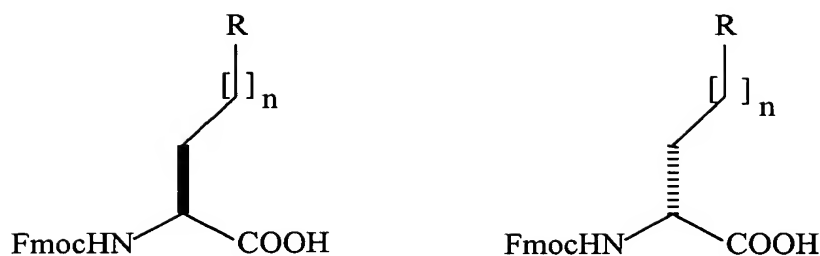
R=COOH, tetazole, CH_2COOH , 4-NHSO₂CH₃, 4-NHSO₂Phenyl, 4-CH₂SO₃H, SO₃H, 4-CH₂PO₃H₂, CH₂CH₂COOH, OCH₂Tetrazole, CH₂STetrazole, HNTetrazole, CONHSO₂R₁ where R₁ is CH₃ or Phenyl SO₂-Tetrazole, CH₂CH₂SO₃H, 1,2,4-tetrazole, 3-isoxazolone, amidotetrazole, CH₂CH₂PO₃H₂

Scheme 1



R = COOH, tetrazole, CH_2COOH , CH₂tetrazole

Scheme 2



R = COOH, tetazole, CH₂COOH, 4-NHSO₂CH₃, 4-NHSO₂Phenyl, 4-CH₂SO₃H, SO₃H, 4-CH₂PO₃H₂, CH₂CH₂COOH, OCH₂Tetrazole, CH₂STetrazole, HNTetrazole, CONHSO₂R₁ where R₁ is CH₃ or Phenyl SO₂-Tetrazole, CH₂CH₂SO₃H, 1,2,4-tetrazole, 3-isoxazolone, amidotetrazole, CH₂CH₂PO₃H₂ n = 0, 1, 2, or 3

Scheme 3

[0016] Optionally, in the conotoxin peptides of the present invention, the Asn residues may be modified to contain an N-glycan and the Ser, Thr and Hyp residues may be modified to contain an O-glycan (e.g., g-N, g-S, g-T and g-Hyp). In accordance with the present invention, a glycan shall mean any N-, S- or O-linked mono-, di-, tri-, poly- or oligosaccharide that can be attached to any hydroxy, amino or thiol group of natural or modified amino acids by synthetic or enzymatic methodologies known in the art. The monosaccharides making up the glycan can include D-allose, D-altrose, D-glucose, D-mannose, D-gulose, D-idose, D-galactose, D-talose, D-galactosamine, D-glucosamine, D-N-acetyl-glucosamine (GlcNAc), D-N-acetyl-galactosamine (GalNAc), D-fucose or D-arabinose. These saccharides may be structurally modified, e.g., with one or more O-sulfate, O-phosphate, O-acetyl or acidic groups, such as sialic acid, including combinations thereof. The glycan may also include similar polyhydroxy groups, such as D-penicillamine 2,5 and halogenated derivatives thereof or polypropylene glycol derivatives. The glycosidic linkage is beta and 1-4 or 1-3, preferably 1-3. The linkage between the glycan and the amino acid may be alpha or beta, preferably alpha and is 1-.

[0017] Core O-glycans have been described by Van de Steen et al. (1998), incorporated herein by reference. Mucin type O-linked oligosaccharides are attached to Ser or Thr (or other hydroxylated residues of the present peptides) by a GalNAc residue. The monosaccharide building blocks and the linkage attached to this first GalNAc residue define the "core glycans," of which eight have been identified. The type of glycosidic linkage (orientation and

connectivities) are defined for each core glycan. Suitable glycans and glycan analogs are described further in U.S. Serial No. 09/420,797 filed 19 October 1999 and in PCT Application No. PCT/US99/24380 filed 19 October 1999 (PCT Published Application No. WO 00/23092), each incorporated herein by reference. A preferred glycan is Gal(β 1 \rightarrow 3)GalNAc(α 1 \rightarrow).

5 [0018] Optionally, in the conotoxin peptides described above, pairs of Cys residues may be replaced pairwise with isoteric lactam or ester-thioether replacements, such as Ser/(Glu or Asp), Lys/(Glu or Asp), Cys/(Glu or Asp) or Cys/Ala combinations. Sequential coupling by known methods (Barnay et al., 2000; Hruby et al., 1994; Bitan et al., 1997) allows replacement of native Cys bridges with lactam bridges. Thioether analogs may be readily synthesized using halo-Ala residues commercially available from RSP Amino Acid Analogues. In addition, individual Cys residues may be replaced with homoCys, seleno-Cys or penicillamine, so that disulfide bridges may be formed between Cys-homoCys or Cys-penicillamine, or homoCys-penicillamine and the like.

[0019] The present invention is further directed to derivatives of the above peptides and peptide derivatives which are acyclic permutations in which the cyclic permutants retain the native bridging pattern of native toxin. See, Craik et al. (2001).

[0020] The present invention is further directed to a method of treating disorders associated with voltage-gated ion channels, ligand-gated ion channels and/or receptor disorders in a subject comprising administering to the subject an effective amount of the pharmaceutical composition comprising a therapeutically effective amount of a conotoxin peptide described
20 herein or a pharmaceutically acceptable salt or solvate thereof. The present invention is also directed to a pharmaceutical composition comprising a therapeutically effective amount of a conotoxin peptide described herein or a pharmaceutically acceptable salt or solvate thereof and a pharmaceutically acceptable carrier.

25 [0021] More specifically, the present invention is also directed to nucleic acids which encode conotoxin peptides of the present invention or which encodes precursor peptides for these conotoxin peptides, as well as the precursor peptide. The nucleic acid sequences encoding the precursor peptides of other conotoxin peptides of the present invention are set forth in Table 1. Table 1 also sets forth the amino acid sequences of these precursor peptides.

30 [0022] Another embodiment of the invention contemplates a method of identifying compounds that mimic the therapeutic activity of the instant peptide, comprising the steps of: (a) conducting a biological assay on a test compound to determine the therapeutic activity; and (b)

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comparing the results obtained from the biological assay of the test compound to the results obtained from the biological assay of the peptide. The peptide is labeled with any conventional label, preferably a radioiodine on an available Tyr. Thus, the invention is also directed to radioiodinated conotoxins.

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DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

[0023] The present invention is directed to conotoxin peptides, derivatives or pharmaceutically acceptable salts thereof. The present invention is further directed to the use of this peptide, derivatives thereof and pharmaceutically acceptable salts thereof for the treatment of disorders associated with voltage-gated ion channels, ligand-gated ion channels and/or receptors. The invention is further directed to nucleic acid sequences encoding the conotoxin peptides and encoding propeptides, as well as the propeptides.

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[0024] The present invention, in another aspect, relates to a pharmaceutical composition comprising an effective amount of a conotoxin peptides, a mutein thereof, an analog thereof, an active fragment thereof or pharmaceutically acceptable salts or solvates. Such a pharmaceutical composition has the capability of acting at voltage-gated ion channels, ligand-gated ion channels and/or receptors, and are thus useful for treating a disorder or disease of a living animal body, including a human, which disorder or disease is responsive to the partial or complete blockade of such channels or receptors comprising the step of administering to such a living animal body, including a human, in need thereof a therapeutically effective amount of a pharmaceutical composition of the present invention.

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[0025] Examples of voltage-gated ion channels include the voltage-gated calcium channel, the voltage-gated sodium channel, the voltage-gated potassium channel and the proton-gated ion channel. Examples of ligand-gated channels include the nicotinic ligand-gated ion channel, ligand-gated glutamate (NMDA) channel and the ligand-gated 5HT₃ (serotonin) channel. Examples of receptors include the G-protein receptors. Activity of ψ -conotoxins is described in U.S. Patent No. 5,969,096 and in Shon et al. (1997). Activity of bromosleeper conotoxins is described in U.S. Patent No. 5,889,147 and in Craig et al. (1997). Activity of σ -conotoxins is described in U.S. Patent No. 5,889,147. Activity of contryphan conotoxins is described in U.S. Patent No. 6,077,934 and in Jimenez et al. (1996). Activity of conopressins is described in Cruz et al. (1987) and in Kruszynski et al. (1990). Activity of γ -conotoxins is described in Fainzilber et al. (1998). Activity of α A-conotoxins (kappaA??) is described in

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Jacobsen et al. (1997) and in Hopkins et al. (1995). Activity of α -conotoxins is described in U.S. Patent Nos. 4,447,356 and 5,514,774. Activity of τ -conotoxins is described in U.S. Serial No. 09/497,491 (PCT/US00/03021, PCT published application WO 00/46371) as an antagonist for acetylcholine receptors and as analgesic agents for the treatment of pain (whether acute or chronic), including migraine, chronic pain, and neuropathic pain, without undesirable side effects. Activity of contulakins is described in U.S. Serial No. 09/420,797 (PCT/US99/24380, PCT published application WO 00/23092). Each of these references is incorporated herein by reference.

[0026] Since σ -conotoxins are antagonists of the 5HT₃ receptor, they are also useful in treating irritable bowel syndrome (IBS) and visceral pain. Visceral pain is a common experience in health and disease. Chronic visceral hyperalgesia in the absence of detectable organic disease has been implicated in many common functional bowel disorders (FDB), such as IBS, non-ulcer dyspepsia (NUD) and non-cardiac chest pain (NCCP).

[0027] Pain in IBS cannot be explained by normal perception of abnormal motility. In the majority of patients, sensory perception itself is abnormal. Most visceral afferent information is part of the reflex activity of digestion and does not reach conscious perception. Increasing evidence suggests that long term changes in the thresholds and gain of the visceral afferent pathways are present in patients with FDBs. This has been referred to as visceral hyperalgesia (Mayer et al., 1994).

[0028] It has been proposed that FDBs are a result of increased excitability of spinal neurones. According to their model, many inputs can result in transient, short term, or life long sensitization of afferent pathways involved in visceral reflexes and sensations from the gut. The increased sensory input to interneurons and / or dorsal horn neurons in the spinal cord will result in secondary hyperalgesia, in which adjacent, undamaged viscera develop sensitivity to normal innocuous stimuli (allodynia), and central hyperexcitability as a consequence of changes in the circuitry of the dorsal horn. This central sensitization may subsequently extend to supraspinal centers also.

[0029] Altered spinal processing of visceral sensory information can explain altered sensory thresholds and altered referral patterns, the perception of visceral sensations without stimulation of visceral mechanoreceptors (sensation of incomplete evacuation), and the symptomatic involvement of multiple sites in the GI tract, including extra intestinal sites. Increased excitability of dorsal horn neurones, resulting in the recruitment of previously sub-

threshold inputs, may explain cutaneous allodynia in some patients with IBS, burning sensations referred to different parts of the body, cold hypersensitivity and pain referral to upper and lower extremities.

[0030] A number of compounds have been shown to modulate visceral sensitivity in IBS patients. These include octreotide (sst₂; Novartis), the 5-HT₃ antagonists odansetron (Glaxo) and granisetron (SKB) and the peripheral kappa opioid agonist, fedotozine (Jouveinal SA). The 5-HT₃ antagonist alosteron (Glaxo), currently in development for IBS, is active in modifying the perception of colonic distension and gut compliance in IBS patients. New drugs in development for the treatment of IBS that are targeted at pain control as well as dysmotility include 5-HT₃ and 5-HT₄ receptor antagonists. 5-HT₃ receptors are located throughout the central and peripheral nervous system – their role in modulating the activity of visceral afferent and enteric neurones has led to the proposal that 5-HT acts as a sensitizing agent via these receptors on visceral afferent neurones. 5-HT₃ receptor antagonists have been widely reported to attenuate blood pressure responses to intestinal distension. 5-HT₃ antagonists in development for IBS include Alosteron (phase III), which is reported to reduce abdominal pain, slow colonic transit and increase colon compliance in IBS patients. Other compounds with positive effects include the antiemetic Ramosteron (Yamanouchi), Cilansteron (Solvay) and YM-114 (Yamanouchi). An animal model for dysmotility of the GI tract has been described by Maric et al. (1989).

[0031] The conotoxin peptides described herein are sufficiently small to be chemically synthesized. General chemical syntheses for preparing the foregoing conotoxin peptides are described hereinafter. Various ones of the conotoxin peptides can also be obtained by isolation and purification from specific *Conus* species using the technique described in U.S. Patent Nos. 4,447,356 (Olivera et al., 1984); 5,514,774; 5,719,264; and 5,591,821, as well as in PCT published application WO 98/03189, the disclosures of which are incorporated herein by reference.

[0032] Although the conotoxin peptides of the present invention can be obtained by purification from cone snails, because the amounts of conotoxin peptides obtainable from individual snails are very small, the desired substantially pure conotoxin peptides are best practically obtained in commercially valuable amounts by chemical synthesis using solid-phase strategy. For example, the yield from a single cone snail may be about 10 micrograms or less of conotoxin peptides peptide. By "substantially pure" is meant that the peptide is present in the substantial absence of other biological molecules of the same type; it is preferably present in an

amount of at least about 85% purity and preferably at least about 95% purity. Chemical synthesis of biologically active conotoxin peptides depends of course upon correct determination of the amino acid sequence.

[0033] The conotoxin peptides can also be produced by recombinant DNA techniques well known in the art. Such techniques are described by Sambrook et al. (1989). A gene of interest (i.e., a gene that encodes a suitable conotoxin peptides) can be inserted into a cloning site of a suitable expression vector by using standard techniques. These techniques are well known to those skilled in the art. The expression vector containing the gene of interest may then be used to transfect the desired cell line. Standard transfection techniques such as calcium phosphate co-precipitation, DEAE-dextran transfection or electroporation may be utilized. A wide variety of host/expression vector combinations may be used to express a gene encoding a conotoxin peptide of interest. Such combinations are well known to a skilled artisan. The peptides produced in this manner are isolated, reduced if necessary, and oxidized to form the correct disulfide bonds.

[0034] One method of forming disulfide bonds in the conotoxin peptides of the present invention is the air oxidation of the linear peptides for prolonged periods under cold room temperatures or at room temperature. This procedure results in the creation of a substantial amount of the bioactive, disulfide-linked peptides. The oxidized peptides are fractionated using reverse-phase high performance liquid chromatography (HPLC) or the like, to separate peptides having different linked configurations. Thereafter, either by comparing these fractions with the elution of the native material or by using a simple assay, the particular fraction having the correct linkage for maximum biological potency is easily determined. However, because of the dilution resulting from the presence of other fractions of less biopotency, a somewhat higher dosage may be required.

[0035] The peptides are synthesized by a suitable method, such as by exclusively solid-phase techniques, by partial solid-phase techniques, by fragment condensation or by classical solution couplings.

[0036] In conventional solution phase peptide synthesis, the peptide chain can be prepared by a series of coupling reactions in which constituent amino acids are added to the growing peptide chain in the desired sequence. Use of various coupling reagents, e.g., dicyclohexylcarbodiimide or diisopropylcarbonyldimidazole, various active esters, e.g., esters of N-hydroxyphthalimide or N-hydroxy-succinimide, and the various cleavage reagents, to carry

out reaction in solution, with subsequent isolation and purification of intermediates, is well known classical peptide methodology. Classical solution synthesis is described in detail in the treatise, "Methoden der Organischen Chemie (Houben-Weyl): Synthese von Peptiden," (1974). Techniques of exclusively solid-phase synthesis are set forth in the textbook, "Solid-Phase Peptide Synthesis," (Stewart and Young, 1969), and are exemplified by the disclosure of U.S. Patent 4,105,603 (Vale et al., 1978). The fragment condensation method of synthesis is exemplified in U.S. Patent 3,972,859 (1976). Other available syntheses are exemplified by U.S. Patents No. 3,842,067 (1974) and 3,862,925 (1975). The synthesis of peptides containing γ -carboxyglutamic acid residues is exemplified by Rivier et al. (1987), Nishiuchi et al. (1993) and Zhou et al. (1996).

[0037] Common to such chemical syntheses is the protection of the labile side chain groups of the various amino acid moieties with suitable protecting groups which will prevent a chemical reaction from occurring at that site until the group is ultimately removed. Usually also common is the protection of an α -amino group on an amino acid or a fragment while that entity reacts at the carboxyl group, followed by the selective removal of the α -amino protecting group to allow subsequent reaction to take place at that location. Accordingly, it is common that, as a step in such a synthesis, an intermediate compound is produced which includes each of the amino acid residues located in its desired sequence in the peptide chain with appropriate side-chain protecting groups linked to various ones of the residues having labile side chains.

[0038] As far as the selection of a side chain amino protecting group is concerned, generally one is chosen which is not removed during deprotection of the α -amino groups during the synthesis. However, for some amino acids, e.g., His, protection is not generally necessary. In selecting a particular side chain protecting group to be used in the synthesis of the peptides, the following general rules are followed: (a) the protecting group preferably retains its protecting properties and is not split off under coupling conditions, (b) the protecting group should be stable under the reaction conditions selected for removing the α -amino protecting group at each step of the synthesis, and (c) the side chain protecting group must be removable, upon the completion of the synthesis containing the desired amino acid sequence, under reaction conditions that will not undesirably alter the peptide chain.

[0039] It should be possible to prepare many, or even all, of these peptides using recombinant DNA technology. However, when peptides are not so prepared, they are preferably prepared using the Merrifield solid-phase synthesis, although other equivalent chemical

syntheses known in the art can also be used as previously mentioned. Solid-phase synthesis is commenced from the C-terminus of the peptide by coupling a protected α -amino acid to a suitable resin. Such a starting material can be prepared by attaching an α -amino-protected amino acid by an ester linkage to a chloromethylated resin or a hydroxymethyl resin, or by an amide bond to a benzhydrylamine (BHA) resin or paramethylbenzhydrylamine (MBHA) resin. Preparation of the hydroxymethyl resin is described by Bodansky et al. (1966). Chloromethylated resins are commercially available from Bio Rad Laboratories (Richmond, CA) and from Lab. Systems, Inc. The preparation of such a resin is described by Stewart and Young (1969). BHA and MBHA resin supports are commercially available, and are generally used when the desired polypeptide being synthesized has an unsubstituted amide at the C-terminus. Thus, solid resin supports may be any of those known in the art, such as one having the formulae $-O-CH_2$ -resin support, $-NH$ BHA resin support, or $-NH$ -MBHA resin support. When the unsubstituted amide is desired, use of a BHA or MBHA resin is preferred, because cleavage directly gives the amide. In case the N-methyl amide is desired, it can be generated from an N-methyl BHA resin. Should other substituted amides be desired, the teaching of U.S. Patent No. 4,569,967 (Kornreich et al., 1986) can be used, or should still other groups than the free acid be desired at the C-terminus, it may be preferable to synthesize the peptide using classical methods as set forth in the Houben-Weyl text (1974).

[0040] The C-terminal amino acid, protected by Boc or Fmoc and by a side-chain protecting group, if appropriate, can be first coupled to a chloromethylated resin according to the procedure set forth in K. Horiki et al. (1978), using KF in DMF at about 60°C for 24 hours with stirring, when a peptide having free acid at the C-terminus is to be synthesized. Following the coupling of the BOC-protected amino acid to the resin support, the α -amino protecting group is removed, as by using trifluoroacetic acid (TFA) in methylene chloride or TFA alone. The deprotection is carried out at a temperature between about 0°C and room temperature. Other standard cleaving reagents, such as HCl in dioxane, and conditions for removal of specific α -amino protecting groups may be used as described in Schroder & Lubke (1965).

[0041] After removal of the α -amino-protecting group, the remaining α -amino- and side chain-protected amino acids are coupled step-wise in the desired order to obtain the intermediate compound defined hereinbefore, or as an alternative to adding each amino acid separately in the synthesis, some of them may be coupled to one another prior to addition to the solid phase reactor. Selection of an appropriate coupling reagent is within the skill of the art. Particularly

suitable as a coupling reagent is N,N'-dicyclohexylcarbodiimide (DCC, DIC, HBTU, HATU, TBTU in the presence of HoBt or HoAt).

[0042] The activating reagents used in the solid phase synthesis of the peptides are well known in the peptide art. Examples of suitable activating reagents are carbodiimides, such as N,N'-diisopropylcarbodiimide and N-ethyl-N'-(3-dimethylaminopropyl)carbodiimide. Other activating reagents and their use in peptide coupling are described by Schroder & Lubke (1965) and Kapoor (1970).

[0043] Each protected amino acid or amino acid sequence is introduced into the solid-phase reactor in about a twofold or more excess, and the coupling may be carried out in a medium of dimethylformamide (DMF):CH₂Cl₂ (1:1) or in DMF or CH₂Cl₂ alone. In cases where intermediate coupling occurs, the coupling procedure is repeated before removal of the α-amino protecting group prior to the coupling of the next amino acid. The success of the coupling reaction at each stage of the synthesis, if performed manually, is preferably monitored by the ninhydrin reaction, as described by Kaiser et al. (1970). Coupling reactions can be performed automatically, as on a Beckman 990 automatic synthesizer, using a program such as that reported in Rivier et al. (1978).

[0044] After the desired amino acid sequence has been completed, the intermediate peptide can be removed from the resin support by treatment with a reagent, such as liquid hydrogen fluoride or TFA (if using Fmoc chemistry), which not only cleaves the peptide from the resin but also cleaves all remaining side chain protecting groups and also the α-amino protecting group at the N-terminus if it was not previously removed to obtain the peptide in the form of the free acid. If Met is present in the sequence, the Boc protecting group is preferably first removed using trifluoroacetic acid (TFA)/ethanedithiol prior to cleaving the peptide from the resin with HF to eliminate potential S-alkylation. When using hydrogen fluoride or TFA for cleaving, one or more scavengers such as anisole, cresol, dimethyl sulfide and methylethyl sulfide are included in the reaction vessel.

[0045] Cyclization of the linear peptide is preferably affected, as opposed to cyclizing the peptide while a part of the peptido-resin, to create bonds between Cys residues. To effect such a disulfide cyclizing linkage, fully protected peptide can be cleaved from a hydroxymethylated resin or a chloromethylated resin support by ammonolysis, as is well known in the art, to yield the fully protected amide intermediate, which is thereafter suitably cyclized and deprotected. Alternatively, deprotection, as well as cleavage of the peptide from the above

resins or a benzhydrylamine (BHA) resin or a methylbenzhydrylamine (MBHA), can take place at 0°C with hydrofluoric acid (HF) or TFA, followed by oxidation as described above.

[0046] The peptides are also synthesized using an automatic synthesizer. Amino acids are sequentially coupled to an MBHA Rink resin (typically 100 mg of resin) beginning at the C-terminus using an Advanced Chemtech 357 Automatic Peptide Synthesizer. Couplings are carried out using 1,3-diisopropylcarbodiimide in N-methylpyrrolidinone (NMP) or by 2-(1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HBTU) and diethylisopropylethylamine (DIEA). The Fmoc protecting group is removed by treatment with a 20% solution of piperidine in dimethylformamide (DMF). Resins are subsequently washed with DMF (twice), followed by methanol and NMP.

[0047] Muteins, analogs or active fragments, of the foregoing conotoxin peptides are also contemplated here. See, e.g., Hammerland et al. (1992). Derivative muteins, analogs or active fragments of the conotoxin peptides may be synthesized according to known techniques, including conservative amino acid substitutions, such as outlined in U.S. Patent Nos. 5,545,723 (see particularly col. 2, line 50--col. 3, line 8); 5,534,615 (see particularly col. 19, line 45--col. 22, line 33); and 5,364,769 (see particularly col. 4, line 55--col. 7, line 26), each herein incorporated by reference.

[0048] Pharmaceutical compositions containing a compound of the present invention as the active ingredient can be prepared according to conventional pharmaceutical compounding techniques. See, for example, *Remington's Pharmaceutical Sciences*, 18th Ed. (1990, Mack Publishing Co., Easton, PA). Typically, an antagonistic amount of active ingredient will be admixed with a pharmaceutically acceptable carrier. The carrier may take a wide variety of forms depending on the form of preparation desired for administration, e.g., intravenous, oral, parenteral or intrathecally. For examples of delivery methods see U.S. Patent No. 5,844,077, incorporated herein by reference.

[0049] "Pharmaceutical composition" means physically discrete coherent portions suitable for medical administration. "Pharmaceutical composition in dosage unit form" means physically discrete coherent units suitable for medical administration, each containing a daily dose or a multiple (up to four times) or a sub-multiple (down to a fortieth) of a daily dose of the active compound in association with a carrier and/or enclosed within an envelope. Whether the composition contains a daily dose, or for example, a half, a third or a quarter of a daily dose, will

depend on whether the pharmaceutical composition is to be administered once or, for example, twice, three times or four times a day, respectively.

[0050] The term "salt", as used herein, denotes acidic and/or basic salts, formed with inorganic or organic acids and/or bases, preferably basic salts. While pharmaceutically acceptable salts are preferred, particularly when employing the compounds of the invention as medicaments, other salts find utility, for example, in processing these compounds, or where non-medicament-type uses are contemplated. Salts of these compounds may be prepared by art-recognized techniques.

[0051] Examples of such pharmaceutically acceptable salts include, but are not limited to, inorganic and organic addition salts, such as hydrochloride, sulphates, nitrates or phosphates and acetates, trifluoroacetates, propionates, succinates, benzoates, citrates, tartrates, fumarates, maleates, methane-sulfonates, isothionates, theophylline acetates, salicylates, respectively, or the like. Lower alkyl quaternary ammonium salts and the like are suitable, as well.

[0052] As used herein, the term "pharmaceutically acceptable" carrier means a non-toxic, inert solid, semi-solid liquid filler, diluent, encapsulating material, formulation auxiliary of any type, or simply a sterile aqueous medium, such as saline. Some examples of the materials that can serve as pharmaceutically acceptable carriers are sugars, such as lactose, glucose and sucrose, starches such as corn starch and potato starch, cellulose and its derivatives such as sodium carboxymethyl cellulose, ethyl cellulose and cellulose acetate; powdered tragacanth; malt, gelatin, talc; excipients such as cocoa butter and suppository waxes; oils such as peanut oil, cottonseed oil, safflower oil, sesame oil, olive oil, corn oil and soybean oil; glycols, such as propylene glycol, polyols such as glycerin, sorbitol, mannitol and polyethylene glycol; esters such as ethyl oleate and ethyl laurate, agar; buffering agents such as magnesium hydroxide and aluminum hydroxide; alginic acid; pyrogen-free water; isotonic saline, Ringer's solution; ethyl alcohol and phosphate buffer solutions, as well as other non-toxic compatible substances used in pharmaceutical formulations.

[0053] Wetting agents, emulsifiers and lubricants such as sodium lauryl sulfate and magnesium stearate, as well as coloring agents, releasing agents, coating agents, sweetening, flavoring and perfuming agents, preservatives and antioxidants can also be present in the composition, according to the judgment of the formulator. Examples of pharmaceutically acceptable antioxidants include, but are not limited to, water soluble antioxidants such as ascorbic acid, cysteine hydrochloride, sodium bisulfite, sodium metabisulfite, sodium sulfite,

and the like; oil soluble antioxidants, such as ascorbyl palmitate, butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), lecithin, propyl gallate, aloha-tocopherol and the like; and the metal chelating agents such as citric acid, ethylenediamine tetraacetic acid (EDTA), sorbitol, tartaric acid, phosphoric acid and the like.

5 [0054] For oral administration, the compounds can be formulated into solid or liquid preparations such as capsules, pills, tablets, lozenges, melts, powders, suspensions or emulsions.

In preparing the compositions in oral dosage form, any of the usual pharmaceutical media may be employed, such as, for example, water, glycols, oils, alcohols, flavoring agents, preservatives, coloring agents, suspending agents, and the like in the case of oral liquid preparations (such as, for example, suspensions, elixirs and solutions); or carriers such as starches, sugars, diluents, granulating agents, lubricants, binders, disintegrating agents and the like in the case of oral solid preparations (such as, for example, powders, capsules and tablets). Because of their ease in administration, tablets and capsules represent the most advantageous oral dosage unit form, in which case solid pharmaceutical carriers are obviously employed. If desired, tablets may be sugar-coated or enteric-coated by standard techniques. The active agent can be encapsulated to make it stable to passage through the gastrointestinal tract while at the same time allowing for passage across the blood brain barrier. See for example, WO 96/11698.

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20 [0055] For parenteral administration, the compound may be dissolved in a pharmaceutical carrier and administered as either a solution or a suspension. Illustrative of suitable carriers are water, saline, dextrose solutions, fructose solutions, ethanol, or oils of animal, vegetative or synthetic origin. The carrier may also contain other ingredients, for example, preservatives, suspending agents, solubilizing agents, buffers and the like. When the compounds are being administered intrathecally, they may also be dissolved in cerebrospinal fluid.

25 [0056] A variety of administration routes are available. The particular mode selected will depend of course, upon the particular drug selected, the severity of the disease state being treated and the dosage required for therapeutic efficacy. The methods of this invention, generally speaking, may be practiced using any mode of administration that is medically acceptable, meaning any mode that produces effective levels of the active compounds without causing
30 clinically unacceptable adverse effects. Such modes of administration include oral, rectal, sublingual, topical, nasal, transdermal or parenteral routes. The term "parenteral" includes subcutaneous, intravenous, epidural, irrigation, intramuscular, release pumps, or infusion.

[0057] For example, administration of the active agent according to this invention may be achieved using any suitable delivery means, including:

- (a) pump (see, e.g., Luer & Hatton (1993), Zimm et al. (1984) and Ettinger et al. (1978));
- (b), microencapsulation (see, e.g., U.S. Patent Nos. 4,352,883; 4,353,888; and 5,084,350);
- (c) continuous release polymer implants (see, e.g., U.S. Patent No. 4,883,666);
- (d) macroencapsulation (see, e.g., U.S. Patent Nos. 5,284,761, 5,158,881, 4,976,859 and 4,968,733 and published PCT patent applications WO92/19195, WO 95/05452);
- (e) naked or unencapsulated cell grafts to the CNS (see, e.g., U.S. Patent Nos. 5,082,670 and 5,618,531);
- (f) injection, either subcutaneously, intravenously, intra-arterially, intramuscularly, or to other suitable site; or
- (g) oral administration, in capsule, liquid, tablet, pill, or prolonged release formulation.

[0058] In one embodiment of this invention, an active agent is delivered directly into the CNS, preferably to the brain ventricles, brain parenchyma, the intrathecal space or other suitable CNS location, most preferably intrathecally.

[0059] Alternatively, targeting therapies may be used to deliver the active agent more specifically to certain types of cell, by the use of targeting systems such as antibodies or cell specific ligands. Targeting may be desirable for a variety of reasons, e.g. if the agent is unacceptably toxic, or if it would otherwise require too high a dosage, or if it would not otherwise be able to enter the target cells.

[0060] The active agents, which are peptides, can also be administered in a cell based delivery system in which a DNA sequence encoding an active agent is introduced into cells designed for implantation in the body of the patient, especially in the spinal cord region. Suitable delivery systems are described in U.S. Patent No. 5,550,050 and published PCT Application Nos. WO 92/19195, WO 94/25503, WO 95/01203, WO 95/05452, WO 96/02286, WO 96/02646, WO 96/40871, WO 96/40959 and WO 97/12635. Suitable DNA sequences can be prepared synthetically for each active agent on the basis of the developed sequences and the known genetic code.

[0061] Exemplary methods for administering such muscle relaxant compounds (e.g., so as to achieve sterile or aseptic conditions) will be apparent to the skilled artisan. Certain methods suitable for administering compounds useful according to the present invention are set

forth in Goodman and Gilman's *The Pharmacological Basis of Therapeutics*, 7th Ed. (1985). The administration to the patient can be intermittent; or at a gradual, continuous, constant or controlled rate. Administration can be to a warm-blooded animal (e.g. a mammal, such as a mouse, rat, cat, rabbit, dog, pig, cow or monkey); but advantageously is administered to a human being. Administration occurs after general anesthesia is administered. The frequency of administration normally is determined by an anesthesiologist, and typically varies from patient to patient.

[0062] The active agent is preferably administered in an therapeutically effective amount. By a "therapeutically effective amount" or simply "effective amount" of an active compound is meant a sufficient amount of the compound to treat the desired condition at a reasonable benefit/risk ratio applicable to any medical treatment. The actual amount administered, and the rate and time-course of administration, will depend on the nature and severity of the condition being treated. Prescription of treatment, e.g. decisions on dosage, timing, etc., is within the responsibility of general practitioners or specialists, and typically takes account of the disorder to be treated, the condition of the individual patient, the site of delivery, the method of administration and other factors known to practitioners. Examples of techniques and protocols can be found in *Remington's Pharmaceutical Sciences*.

[0063] Dosage may be adjusted appropriately to achieve desired drug levels, locally or systemically. Typically the active agents of the present invention exhibit their effect at a dosage range from about 0.001 mg/kg to about 250 mg/kg, preferably from about 0.01 mg/kg to about 100 mg/kg of the active ingredient, more preferably from about 0.05 mg/kg to about 75 mg/kg. A suitable dose can be administered in multiple sub-doses per day. Typically, a dose or sub-dose may contain from about 0.1 mg to about 500 mg of the active ingredient per unit dosage form. A more preferred dosage will contain from about 0.5 mg to about 100 mg of active ingredient per unit dosage form. Dosages are generally initiated at lower levels and increased until desired effects are achieved. In the event that the response in a subject is insufficient at such doses, even higher doses (or effective higher doses by a different, more localized delivery route) may be employed to the extent that patient tolerance permits. Continuous dosing over, for example 24 hours or multiple doses per day are contemplated to achieve appropriate systemic levels of compounds.

[0064] Advantageously, the compositions are formulated as dosage units, each unit being adapted to supply a fixed dose of active ingredients. Tablets, coated tablets, capsules, ampoules and suppositories are examples of dosage forms according to the invention.

[0065] It is only necessary that the active ingredient constitute an effective amount, i.e., such that a suitable effective dosage will be consistent with the dosage form employed in single or multiple unit doses. The exact individual dosages, as well as daily dosages, are determined according to standard medical principles under the direction of a physician or veterinarian for use humans or animals.

[0066] The pharmaceutical compositions will generally contain from about 0.0001 to 99 wt. %, preferably about 0.001 to 50 wt. %, more preferably about 0.01 to 10 wt.% of the active ingredient by weight of the total composition. In addition to the active agent, the pharmaceutical compositions and medicaments can also contain other pharmaceutically active compounds. Examples of other pharmaceutically active compounds include, but are not limited to, analgesic agents, cytokines and therapeutic agents in all of the major areas of clinical medicine. When used with other pharmaceutically active compounds, the conopeptides of the present invention may be delivered in the form of drug cocktails. A cocktail is a mixture of any one of the compounds useful with this invention with another drug or agent. In this embodiment, a common administration vehicle (e.g., pill, tablet, implant, pump, injectable solution, etc.) would contain both the instant composition in combination supplementary potentiating agent. The individual drugs of the cocktail are each administered in therapeutically effective amounts. A therapeutically effective amount will be determined by the parameters described above; but, in any event, is that amount which establishes a level of the drugs in the area of body where the drugs are required for a period of time which is effective in attaining the desired effects.

[0067] The present invention also relates to rational drug design for the identification of additional drugs which can be used for the purposes described herein. The goal of rational drug design is to produce structural analogs of biologically active polypeptides of interest or of small molecules with which they interact (e.g., agonists, antagonists, inhibitors) in order to fashion drugs which are, for example, more active or stable forms of the polypeptide, or which, e.g., enhance or interfere with the function of a polypeptide *in vivo*. Several approaches for use in rational drug design include analysis of three-dimensional structure, alanine scans, molecular modeling and use of anti-id antibodies. These techniques are well known to those skilled in the art. Such techniques may include providing atomic coordinates defining a three-dimensional

structure of a protein complex formed by said first polypeptide and said second polypeptide, and designing or selecting compounds capable of interfering with the interaction between a first polypeptide and a second polypeptide based on said atomic coordinates.

[0068] Following identification of a substance which modulates or affects polypeptide activity, the substance may be further investigated. Furthermore, it may be manufactured and/or used in preparation, i.e., manufacture or formulation, or a composition such as a medicament, pharmaceutical composition or drug. These may be administered to individuals.

[0069] A substance identified as a modulator of polypeptide function may be peptide or non-peptide in nature. Non-peptide "small molecules" are often preferred for many *in vivo* pharmaceutical uses. Accordingly, a mimetic or mimic of the substance (particularly if a peptide) may be designed for pharmaceutical use.

[0070] The designing of mimetics to a known pharmaceutically active compound is a known approach to the development of pharmaceuticals based on a "lead" compound. This approach might be desirable where the active compound is difficult or expensive to synthesize or where it is unsuitable for a particular method of administration, e.g., pure peptides are unsuitable active agents for oral compositions as they tend to be quickly degraded by proteases in the alimentary canal. Mimetic design, synthesis and testing is generally used to avoid randomly screening large numbers of molecules for a target property.

[0071] Once the pharmacophore has been found, its structure is modeled according to its physical properties, e.g., stereochemistry, bonding, size and/or charge, using data from a range of sources, e.g., spectroscopic techniques, x-ray diffraction data and NMR. Computational analysis, similarity mapping (which models the charge and/or volume of a pharmacophore, rather than the bonding between atoms) and other techniques can be used in this modeling process.

[0072] A template molecule is then selected, onto which chemical groups that mimic the pharmacophore can be grafted. The template molecule and the chemical groups grafted thereon can be conveniently selected so that the mimetic is easy to synthesize, is likely to be pharmacologically acceptable, and does not degrade *in vivo*, while retaining the biological activity of the lead compound. Alternatively, where the mimetic is peptide-based, further stability can be achieved by cyclizing the peptide, increasing its rigidity. The mimetic or mimetics found by this approach can then be screened to see whether they have the target

property, or to what extent it is exhibited. Further optimization or modification can then be carried out to arrive at one or more final mimetics for *in vivo* or clinical testing.

[0073] The present invention further relates to the use of a labeled (e.g., radiolabel, fluorophore, chromophore or the like) of the conotoxins described herein as a molecular tool both *in vitro* and *in vivo*, for discovery of small molecules that exert their action at or partially at the same functional site as the native toxin and capable of elucidation similar functional responses as the native toxin. In one embodiment, the displacement of a labeled conotoxin from its receptor or other complex by a candidate drug agent is used to identify suitable candidate drugs. In a second embodiment, a biological assay on a test compound to determine the therapeutic activity is conducted and compared to the results obtained from the biological assay of a conotoxin. In a third embodiment, the binding affinity of a small molecule to the receptor of a conotoxin is measured and compared to the binding affinity of a conotoxin to its receptor.

[0074] The practice of the present invention employs, unless otherwise indicated, conventional techniques of chemistry, molecular biology, microbiology, recombinant DNA, genetics, immunology, cell biology, cell culture and transgenic biology, which are within the skill of the art. See, e.g., Maniatis *et al.*, 1982; Sambrook *et al.*, 1989; Ausubel *et al.*, 1992; Glover, 1985; Anand, 1992; Guthrie and Fink, 1991; Harlow and Lane, 1988; Jakoby and Pastan, 1979; *Nucleic Acid Hybridization* (B. D. Hames & S. J. Higgins eds. 1984); *Transcription And Translation* (B. D. Hames & S. J. Higgins eds. 1984); *Culture Of Animal Cells* (R. I. Freshney, Alan R. Liss, Inc., 1987); *Immobilized Cells And Enzymes* (IRL Press, 1986); B. Perbal, *A Practical Guide To Molecular Cloning* (1984); the treatise, *Methods In Enzymology* (Academic Press, Inc., N.Y.); *Gene Transfer Vectors For Mammalian Cells* (J. H. Miller and M. P. Calos eds., 1987, Cold Spring Harbor Laboratory); *Methods In Enzymology*, Vols. 154 and 155 (Wu et al. eds.), *Immunochemical Methods In Cell And Molecular Biology* (Mayer and Walker, eds., Academic Press, London, 1987); *Handbook Of Experimental Immunology*, Volumes I-IV (D. M. Weir and C. C. Blackwell, eds., 1986); Riott, *Essential Immunology*, 6th Edition, Blackwell Scientific Publications, Oxford, 1988; Hogan et al., *Manipulating the Mouse Embryo*, (Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., 1986).

EXAMPLES

[0075] The present invention is described by reference to the following Examples, which are offered by way of illustration and are not intended to limit the invention in any manner. Standard techniques well known in the art or the techniques specifically described below were utilized.

EXAMPLE 1

Isolation of Conotoxin Peptides

[0076] Crude venom was extracted from venom ducts (Cruz et al., 1976), and the components were purified as previously described (Cartier et al., 1996). The crude extract from venom ducts was purified by reverse phase liquid chromatography (RPLC) using a Vydac C₁₈ semi-preparative column (10 x 250 mm). Further purification of bioactive peaks was done on a Vydac C₁₈ analytical column (4.6 x 220 mm). The effluents were monitored at 220 nm. Peaks were collected, and aliquots were assayed for activity. Throughout purification, HPLC fractions were assayed by means of intracerebral ventricular (i.c.v.) injection into mice (Clark et al., 1981).

[0077] The amino acid sequence of the purified peptides were determined by standard methods. The purified peptides were reduced and alkylated prior to sequencing by automated Edman degradation on an Applied Biosystems 477A Protein Sequencer with a 120A Analyzer (DNA/Peptide Facility, University of Utah) (Martinez et al., 1995; Shon et al., 1994).

[0078] In accordance with this method, the conotoxin peptides described as "isolated" in Table 1 were obtained. These conotoxin peptides, as well as the other conotoxin peptides and the conotoxin peptide precursors set forth in Table 1 are synthesized as described in U.S. Patent No. 5,670,622.

EXAMPLE 2

Isolation of DNA Encoding Conopeptides

[0079] DNA coding for conotoxin peptides was isolated and cloned in accordance with conventional techniques using general procedures well known in the art, such as described in Olivera et al. (1996), including using primers based on the DNA sequence of known conotoxin peptides. For example, primers based on the DNA sequence for the Contulakin-G propeptide were used to identify contulakin homologs. The propeptides of these contulakin homologs are

homologous on the basis of primer amplification, even though the sequence of the mature toxins are not homologous with the Contulakin-G mature toxin. Alternatively, cDNA libraries was prepared from *Conus* venom duct using conventional techniques. DNA from single clones was amplified by conventional techniques using primers which correspond approximately to the M13 universal priming site and the M13 reverse universal priming site. Clones having a size of approximately 300-500 nucleotides were sequenced and screened for similarity in sequence to known conotoxins. The DNA sequences and encoded propeptide sequences are set forth in Table 1. DNA sequences coding for the mature toxin can also be prepared on the basis of the DNA sequences set forth in Table 1. An alignment of the conopeptides of the present invention is set forth in Tables 2-14.

TABLE 1

Name: Af6.1
Species: ammiralis
Cloned: Yes

DNA Sequence:

ATCATGGAGAACTGATAATTCTGCTTCTTGTTGCTGCTGTACTGATGTCGACCCAG
 GCCCTGGTTGAACGTGCTGGAGAAAACCGCTCAAAGGAGAACATCAATTTTTTATT
 AAAAAGAAAGAGAGCTGCTGACAGGGGGATGTGGGGCGATTGCAAAGATGGGTTA
 ACGACATGTTTTGCGCCCTCAGAGTGTTGTTCTGAGGATTGTGAAGGGAGCTGCACG
 ATGTGGTGATGACCTCTGACCACAAGCCATCTGACATCACCCTCTCCTCTTCAGAG
 GCTTCAAG (SEQ ID NO:1)

Translation:

MEKLIILLLVAAVLMSTQALVERAGENRSKENINFLKRAADRGMWGDCKDGLTTC
 FAPSECCSEDCEGSCTMW (SEQ ID NO:2)

Toxin Sequence:

Gly-Met-Xaa4-Gly-Asp-Cys-Lys-Asp-Gly-Leu-Thr-Thr-Cys-Phe-Ala-Xaa3-Ser-Xaa1-Cys-Cys-
 Ser-Xaa1-Asp-Cys-Xaa1-Gly-Ser-Cys-Thr-Met-Xaa4-^ (SEQ ID NO:3)

Name: Af6.2
Species: ammiralis
Cloned: Yes

DNA Sequence:

ATCATGGAGAACTGACAATTCTGCTTCTTGTTGCTGCTGTACTGATGTCGACCCAG
 GCCCTGCCTCAAGGTGGTGGAGAAAAACGCCCAAGGGAGAAATATCAGATTTTTATC
 AAAAAGAAAGACAAATGCTGAGCGTTGGAGGGAGGGCAGTTGCACCTCTTGGTTAG

CGACGTGTACGCAAGACCAGCAATGCTGTACTGATGTTTGTACAAAAGGGACTAC
TGCGCCTTGTGGGATGACCGCTGACCACAAGCCATCTGACATCACCCTCTCCTGTT
CAGAGTCTTCAAG (SEQ ID NO:4)

5 **Translation:**

MEKLTILLLVAAVLMSTQALPQGGGEKRPRENIRFLSKRKTNAERWREGSCTSWLATC
TQDQQCCTDVCYKRDYCALWDDR (SEQ ID NO:5)

Toxin Sequence:

10 Xaa4-Arg-Xaa1-Gly-Ser-Cys-Thr-Ser-Xaa4-Leu-Ala-Thr-Cys-Thr-Gln-Asp-Gln-Gln-Cys-Cys-
Thr-Asp-Val-Cys-Xaa5-Lys-Arg-Asp-Xaa5-Cys-Ala-Leu-Xaa4-Asp-Asp-Arg-^ (SEQ ID NO:6)

Name: Af6.3
Species: ammiralis
Cloned: Yes

DNA Sequence:

ATCATGCAGAAACTGATAATTCTGCTTCTTGTTGCTGCTGTGCTGATGTCGACCCAG
GCCCTGTTTCAAGAAAAACGCACAATGAAGAAGATCGATTTTTTATCAAAGGGAAA
GGCAGATGCTGAGAAGCAGAGGAAGCGCAATTGCTCGGATGATTGGCAGTATTGTG
AAAGTCCCAGTGACTGCTGTAGTTGGGATTGTGATGTGGTCTGCTCGGGATGAACTC
TGACCACAAGTCATCCGACATCACCCTCTCCTGTTTCAGAGGCTTCAAG (SEQ ID
NO:7)

Translation:

MQKLIILLLVAAVLMSTQALFQEKRTMKKIDFLSKGKADAEEKQRKRNCSDDWQYCESP
SDCCSWDCDVVCSG (SEQ ID NO:8)

30 **Toxin Sequence:**

Asn-Cys-Ser-Asp-Asp-Xaa4-Gln-Xaa5-Cys-Xaa1-Ser-Xaa3-Ser-Asp-Cys-Cys-Ser-Xaa4-Asp-
Cys-Asp-Val-Val-Cys-Ser-# (SEQ ID NO:9)

35 **Name:** Af6.4
Species: ammiralis
Cloned: Yes

DNA Sequence:

40 ATCATGCAGAAACTGATAATCCTGCTTCTTGTTGCTGCTCTACTGTTGTCGATCCAG
GCGGTAAATCAAGAAAAACACCAACGGGCAAAGATCAACTTGCTTTCAAAGAGAA
AGCCACCTGCTGAGCGTTGGTGGCGGTGGGGAGGATGCATGGCTTGGTTTGGGAAA
TGTTCTGAAGGACTCGGAATGTTGTTCTAATAGTTGTGACATAACGCGCTGCGAGTTA
ATGCGATTCCCACCAGACTGGTGACATCGACACTCTCCTGTTTCAGAGTCTTCAAG
45 (SEQ ID NO:10)

Translation:

MQKLIHLLLVAALLLSIQAVNQEKHQRAKINLLSKRKPPAERWWRWGGCMAWFGKCS
KDSECCSNSCDITRCELMRFPPDW (SEQ ID NO:11)

Toxin Sequence:

5 Xaa4-Xaa4-Arg-Xaa4-Gly-Gly-Cys-Met-Ala-Xaa4-Phe-Gly-Lys-Cys-Ser-Lys-Asp-Ser-Xaa1-
Cys-Cys-Ser-Asn-Ser-Cys-Asp-Ile-Thr-Arg-Cys-Xaa1-Leu-Met-Arg-Phe-Xaa3-Xaa3-Asp-
Xaa4-^ (SEQ ID NO:12)

10 **Name:** Af6.5
Species: ammiralis
Cloned: Yes

DNA Sequence:

ATCATGGAGAACTGACAATCCTGCTTCTTGTTGCTGCTGTACTGACGTCGACCCAG
GCCCTGATTCAAGGTGGTGGAGACGAACGCCAAAAGGCAAAGATCAACTTTCTTTC
AAGGTCGGACCGCGATTGCAGGGGTTACGATGCGCCGTGTAGCTCTGGCGCGCCAT
GTTGTGATTGGTGGACATGTTTCAGCACGAACCGGGCGCTGTTTTTAGGCTGACCACA
AGCCATCCGACATCACCCTCTCCTCTTCAGAGGCTTCAAG (SEQ ID NO:13)

Translation:

MEKLTILLLVAAVLTSTQALIQGGGDERQKAKINFLSRSDRDCRGYDAPCSSGAPCCDW
WTCSARTGRCF (SEQ ID NO:14)

Toxin Sequence:

25 Asp-Cys-Arg-Gly-Xaa5-Asp-Ala-Xaa3-Cys-Ser-Ser-Gly-Ala-Xaa3-Cys-Cys-Asp-Xaa4-Xaa4-
Thr-Cys-Ser-Ala-Arg-Thr-Gly-Arg-Cys-Phe-^ (SEQ ID NO:15)

30 **Name:** Af6.6
Species: ammiralis
Cloned: Yes

DNA Sequence:

35 ATCATGCAGAACTGACAATTCTGCTTCTTGTTGCTGCTGTGCTGATGTCGACCCAG
GCCGTGCTTCAAGAAAAACGCCCAAAGGAGAAGATCAAGTTTTTATCAAAGAAAAA
GACAGATGCTGAGAAGCAGCAGAAGCGCCTTTGCCCGGATTACACGGAGCCTTGTT
CACATGCCCATGAATGCTGTTCATGGAATTGTCATAATGGGCACTGCACGGGATGA
ACTCGGACCACAAGCCATCGACATCATCACTCTCCTGTTCAGAGTCTTCAAG (SEQ
40 ID NO:16)

Translation:

MQKLTILLLVAAVLMSTQAVLQEKRPKEKIKFLSKKKTD AEKQQKRLCPDYTEPCSHA
HECCSWNCHNGHCTG (SEQ ID NO:17)

Toxin Sequence:

45

Leu-Cys-Xaa3-Asp-Xaa5-Thr-Xaa1-Xaa3-Cys-Ser-His-Ala-His-Xaa1-Cys-Cys-Ser-Xaa4-Asn-Cys-His-Asn-Gly-His-Cys-Thr-# (SEQ ID NO:18)

5 **Name:** Af6.7
Species: ammiralis
Cloned: Yes

DNA Sequence:

10 ATCATGCAGAACTGATAATTCTGCTCCTTGTTGCTGCTGTACTGATGTCGACCCAG
 GCCATGTTTCAAGGTGATGGAGAAAAATCCCGGAAAGCGGAGATCAACTTTTCTAA
 AACAAAGAAATTTGGCGAGAAACAAGCAGAAACGCTGCAGTAGTTGGGCAAAGTATT
 GTGAAGTTGACTCGGAATGCTGTTCCGAACAGTGTGTAAGGTCTTACTGCGCGATGT
 GGTGATGACCTCTGACCACAAGCCATCCGATATCACCCTCTCCTCTTCAGAGACTT
 CAAG (SEQ ID NO:19)

Translation:

MQKLIILLVAAVLMSTQAMFQGDGEKSRKAEINFSKTRNLARNKQKRCSSWAKYCEV
 DSECCSEQCVRSYCAMW (SEQ ID NO:20)

Toxin Sequence:

Cys-Ser-Ser-Xaa4-Ala-Lys-Xaa5-Cys-Xaa1-Val-Asp-Ser-Xaa1-Cys-Cys-Ser-Xaa1-Gln-Cys-Val-Arg-Ser-Xaa5-Cys-Ala-Met-Xaa4-^ (SEQ ID NO:21)

Name: Af9.1
Species: ammiralis
Cloned: Yes

DNA Sequence:

30 GTTAAAATGCATCTGTCACTGGCACGCTCAGCTGTTTTGATGTTGCTTCTGCTGTTTG
 CCTTGGGCAACTTTGTTGTGGTCCAGTCAGGACAGATAACAAGAGATGTGGACAAT
 GGACAGCTCACGGACAACCGCCGTAACCTGCAATCGAAGTGGAAGCCAGTGAGTCT
 CTTTCATGTACGACGGTCTTGTAACAATTCTTGCAATGAGCATTCCGATTGCGAATC
 35 CCATTGTATTTGCACGTTTAGCGGATGCAAAATTATTTTGATATAAACGGATTGAGT
 TTGCTCGTCAACAAGATGTGCGCACTACAGCTCCTCTCTACAGTGTGTACATCGACCA
 AACGACGCATCTTTTATTTCTTTGTCTGTTGTATTTGTTTTCTGTGTTTCATAACGTAC
 AGAGCCCTTTAATTACCTTTACTGCTCTTCACTTAACCTGATAACCGGAAGGTCCAG
 TGCT (SEQ ID NO:22)

Translation:

MHLSLARS AVLMLLLL FALGNFVVVQSGQITRDVDNGQLTDNRRNLQSKWKPVSLFM
 SRRSCNNSCNEHSDCESHCICTFSGCKIILI (SEQ ID NO:23)

Toxin Sequence:

45 Ser-Cys-Asn-Asn-Ser-Cys-Asn-Xaa1-His-Ser-Asp-Cys-Xaa1-Ser-His-Cys-Ile-Cys-Thr-Phe-Ser-Gly-Cys-Lys-Ile-Ile-Leu-Ile-^ (SEQ ID NO:24)

Name: Af9.2
Species: ammiralis
Cloned: Yes

DNA Sequence:

GTAAAAATGCATCTGTCACTGGCACGCTTAGCTGTTTTGATGTTGCTTCTGCTGTTTG
 CCTTGGGCAACTTTGTTGTGGTCCAGTCAGGACAGATAACAAGAGATGTGGACAAT
 GGACAGCTCACGGACAACCGCCGTAACCTGCAATCGAAGTGGAAGCCAGTGAGTCT
 CTTTCATGTACACGACGGTCTTGTAACAATTCTTGCAATGAGCATTCCGATTGCGAATC
 CCATTGTATTTGCACGTTTAGAGGATGCGGAGCTGTTAATGGTTGAGTTTGCTCGTC
 AACATGATGTGCGCACTACACACTACAGCTCCTCTCTACAGTGTGTACATCGACCAAA
 CGACGCATCTTTTATTTCTTTGTCTGTTGTGTTTGTTCCTGTGTTTCATAACGTACAG
 AGCCCTTTAATTACTTTTACTGCTCTTCACTTAACCTGATAACCAGAAGGTCCAGTG
 CT (SEQ ID NO:25)

Translation:

MHLSLARLAVLMLLLFALGNFVVVQSGQITRDVDNGQLTDNRRNLQSKWKPVSLFM
 SRRSCNNSCNEHSDCESHCICTFRGCGAVNG (SEQ ID NO:26)

Toxin Sequence:

Ser-Cys-Asn-Asn-Ser-Cys-Asn-Xaa1-His-Ser-Asp-Cys-Xaa1-Ser-His-Cys-Ile-Cys-Thr-Phe-
 Arg-Gly-Cys-Gly-Ala-Val-Asn-# (SEQ ID NO:27)

Name: Ar6.1
Species: arenatus
Cloned: Yes

DNA Sequence:

ACCAAAACCATCATCAAAATGAAACTGACGTGCGTGGTGATCGTCGCTGTGCTGTTC
 CTGACGGCCTGTCAACTCACTACAGCTGATGACTCCAGAGGTACGCAGAAGCATGG
 TGCCCTGAGATCGACCACCAAACCTCTCCATGTTGACTCGGGGCTGCACGCCTCCTGG
 TGGAGTTTGTGGTTATCATGGTCACTGCTGCGATTTTTCGATACGTTTCGGCAATTTA
 TGTGTGAGTGGCTGACCCGGCATCTGACCTTTCCCCCTTCTTTGCTCCACTATCCTTT
 TTCTGCCTGAGTCCTCCATACCTGAGAGCTGTCATGAACCACTCAACACCTACTCTT
 CCGGAGGTTTCTGAGGAGCTGCATTGAAATAAAAGCCGCATTGC (SEQ ID NO:28)

Translation:

MKLTCVVIVAVLFLTACQLTTADDSRGTQKHGALRSTTKLSMLTRGCTPPGGVCGYHG
 HCCDFCDTFGNLCVSG (SEQ ID NO:29)

Toxin Sequence:

Gly-Cys-Thr-Xaa3-Xaa3-Gly-Gly-Val-Cys-Gly-Xaa5-His-Gly-His-Cys-Cys-Asp-Phe-Cys-Asp-
 Thr-Phe-Gly-Asn-Leu-Cys-Val-Ser-# (SEQ ID NO:30)

Name: Bromosleeper-Ar1
Species: arenatus
Cloned: Yes

DNA Sequence:

GACAGGATTGAACAAAATTCAGGATGTCAGGATTGGGAATCATGGTGCTAACCCCTT
 CTACTTCTTGTGTTTCATGGCAACCAGTCATCAGGATGCAGGAGAGAAGAAGGCGAT
 GCAAAGGGACGCAATCAACGTCAGACGGAGAAGATCACTCACTCGGGGAGTAGTA
 ACTGAGGCGTGCGAAGAGTCCTGTGAGGAGGAGGAAAAGCACTGCTGCCACGTAA
 ATAATGGAGTACCCTCTTGTGCCGTTATATGCTGGGGATAGTTTCTCGCACACTGTC
 TCATTTCATTATTTTATCAGTACAAGTGTAACGAGACATGTCAGAAAGTCGAAGGTT
 GTGCGTATTTGATAAGTATTGTTTACTGGGATGAACGGA (SEQ ID NO:31)

Translation:

MSGLGIMVL TLLLLVFMATSHQDAGEKKAMQRDAINVRRRRSLTRGVVTEACEESCEE
 EEKHCCHVNNGVPSCAVICWG (SEQ ID NO:32)

Toxin Sequence:

Val-Val-Thr-Xaa1-Ala-Cys-Xaa1-Xaa1-Ser-Cys-Xaa1-Xaa1-Xaa1-Lys-His-Cys-Cys-His-
 Val-Asn-Asn-Gly-Val-Xaa3-Ser-Cys-Ala-Val-Ile-Cys-Xaa4-# (SEQ ID NO:33)

Name: Bromosleeper-Ar1A
Species: arenatus
Cloned: Yes

DNA Sequence:

GACAGGATTGAACAAAATTCAGGATGTCAGGATTGGGAATCATGGTGCTAACCCCTT
 CTACTTCTTGTGTTTCATGGCAACCAGTCATCAGGATGCAGGAGAGAAGCAGGCGAC
 GGAAAGGGACGCAATCAACATCAGATGGAGAAGATCACGCACTCGGAGAATAGTA
 ACTGAGGCGTGCGAAGAGTCCTGTGAGGACGAGGAAAAGCACTGCTGCCACGTAA
 ATAATGGAGTACCCTCTTGTGCCGTTATATGCTGGGGATAGTTTCTCGCACACTGTC
 TCATTTCATTATTTTATCAGTACAAGTGTAACGAGACATGTCAGAAAGTCGAAGGTT
 GTGCGTATTTGATAAGTATTGTTTACTGGGATGAACGGA (SEQ ID NO:34)

Translation:

MSGLGIMVL TLLLLVFMATSHQDAGEKQATERDAINIRWRRSRTRRIVTEACEESCEDE
 EKHCHVNNGVPSCAVICWG (SEQ ID NO:35)

Toxin Sequence:

Ile-Val-Thr-Xaa1-Ala-Cys-Xaa1-Xaa1-Ser-Cys-Xaa1-Asp-Xaa1-Xaa1-Lys-His-Cys-Cys-His-
 Val-Asn-Asn-Gly-Val-Xaa3-Ser-Cys-Ala-Val-Ile-Cys-Xaa4-# (SEQ ID NO:36)

Name: Bromosleeper-Ar2
Species: arenatus
Cloned: Yes

5 **DNA Sequence:**

GACAGGATTGAACAAAATTCAGGATGTCAGAACTGGGAATCATGGTGCTAACGCTT
 CTACTTCTTGTGTTCTGGTAACCAAGTCATCAGGATGCAGGAGAGAAGCAGGCGAC
 GGAAAGGGACGCAATCAACATCAGATGGAGAAGATCACTCACTCGGAGAATAGTA
 ACTGAGGCGTGCGAAGAGCACTGTGAGGATGAGGAACAGTTCTGCTGCGGCTTAGA
 10 GAATGGACAACCCTTTTGTGCCCTGTTTGTCTTCGGATAGTTTCTGTACACTGTCTCA
 TTAATTATTTTATCAGTACAAGTGTAACAAAACATGTCAGAAAGTCGAAGGTTGTG
 CGTATTTGATAAGTATTGTTTGCTGGGACGAACGGA (SEQ ID NO:37)

Translation:

MSELGIMVL TLLLLVFLVTSHQDAGEKQATERDAINIRWRRSLTRRIVTEACEEHCEDEE
 QFCCGLENGQPFCAPVCFG (SEQ ID NO:38)

Toxin Sequence:

Ile-Val-Thr-Xaa1-Ala-Cys-Xaa1-Xaa1-His-Cys-Xaa1-Asp-Xaa1-Xaa1-Gln-Phe-Cys-Cys-Gly-
 Leu-Xaa1-Asn-Gly-Gln-Xaa3-Phe-Cys-Ala-Xaa3-Val-Cys-Phe-# (SEQ ID NO:39)

Name: Bromosleeper-Ar3
Species: arenatus
Cloned: Yes

DNA Sequence:

GACAGGATTGAACAAAATTCAGGATGTCAGGATTGGGAATCATGGTGCTAACCCCTT
 CTACTTCTTGTGTTTCATGGCAACCAGTCATCAGGATGCAGGAGAGAAGAAGGTGAT
 30 GCAAAGGGACGCAATCAACGTCAGACGGAGAAGATCACGCACTCGGAGAGTAGTA
 ACTGGGGCGTGCGAAGAGCACTGTGAGGACGAGGAAAAGCACTGCTGCGGCTTAG
 AGAATGGACAACCCTTTTGTGCCCGTCTATGCTTAGGATAGTTTTCTGTACACTGTCT
 TATTCATTATTTTATCAGTACAAGTGAAAACAAAGCATGTCAGAAAGTCGAAGGTTG
 TCGGTATTTGATAAGTATTGTTTACTGGGATGAACGGA (SEQ ID NO:40)

Translation:

MSGLGIMVL TLLLLVFMATSHQDAGEKKVMQRDAINVRRRRSRTRRVVTGACEEHCE
 DEEKHCCGLENGQPF CARLCLG (SEQ ID NO:41)

Toxin Sequence:

Val-Val-Thr-Gly-Ala-Cys-Xaa1-Xaa1-His-Cys-Xaa1-Asp-Xaa1-Xaa1-Lys-His-Cys-Cys-Gly-
 Leu-Xaa1-Asn-Gly-Gln-Xaa3-Phe-Cys-Ala-Arg-Leu-Cys-Leu-# (SEQ ID NO:42)

45 **Name:** C. arenatus contryphan 1
Species: arenatus
Cloned: Yes

DNA Sequence:

ATGGGGAAACTGACAATACTGGTTCTTGTGCTGCTGTACTGTTGTCGACCCAGGTC
 ATGGTTCAAGGTGACGGAGATCAACCTGCAGCTCGCAATGCAGTGCCAAAAGACGA
 5 TAACCCAGATGGAGCGAGTGGAAAGTTCATGAATGTTCTACGTCGGTCTGGATGTC
 CGTGGCATCCTTGGTGTGGCTGATCGGAATCCACGATTGCAATGACAGCC (SEQ ID
 NO:43)

Translation:

10 MGKLTILVLVA AVLSTQVMVQGDGDQPAARNAVPKDDNPDGASGKFMNVLRRSGCP
 WHPWCG (SEQ ID NO:44)

Toxin Sequence:

Ser-Gly-Cys-Xaa3-Xaa4-His-Xaa3-Xaa4-Cys-# (SEQ ID NO:45)

Name: C. arenatus contryphan 1A

Species: arenatus

Cloned: Yes

DNA Sequence:

ATGGGGAAACTGACAATACTGGTTCTTGTGCTGCTGTACTGTTGTCGACCCAGGTC
 ATGGTTCAAGGTGACGGAGATCAACCTGCAGCTCGCAATGCAGTGCCAAAAGACGA
 TAACCCAGATGGAGCGAGTGGAAAGTTCATGAATGTTCTACGTCGGTCTGGATGTC
 25 CGTGGCGCCCTTGGTGTGGCTGATCGGAATCCACGATTGCAATGACAGCC (SEQ ID
 NO:46)

Translation:

30 MGKLTILVLVA AVLSTQVMVQGDGDQPAARNAVPKDDNPDGASGKFMNVLRRSGCP
 WRPWCG (SEQ ID NO:47)

Toxin Sequence:

Ala-Ser-Gly-Cys-Xaa3-Xaa4-Arg-Xaa3-Xaa4-Cys-# (SEQ ID NO:48)

Name: C. arenatus contryphan 2

Species: arenatus

Cloned: Yes

DNA Sequence:

ATGGGGAAACTGACAATACTGGTTCTTGTGCTGCTGTACTGTTGTCGACCCAGGTC
 ATGGTTCAAGGTGACGGAGATCAACCTGCAGGTCGAGATGCAGTTCCAAGAGACGA
 TAACCCAGGTGGAACGAGTGGAAAGTTCATGAATGCTCTACGTCAATATGGATGTC
 45 CGGTGGGTCTTTGGTGTGACTGATCAGAATCCACGATTGCAATGACAGCC (SEQ ID
 NO:49)

Translation:

MGKLTILVLVA AVLSTQVMVQGDGDQPAGRDAVPRDDNPGGTSGKFMNALRQYGC
PVGLWCD (SEQ ID NO:50)

Toxin Sequence:

5 Xaa2-Xaa5-Gly-Cys-Xaa3-Val-Gly-Leu-Xaa4-Cys-Asp-^ (SEQ ID NO:51)

Name: C. arenatus contryphan 4

Species: arenatus

10 **Cloned:** Yes

DNA Sequence:

ATGGGGAAACTGACAATACTGGTTCTTGTTGCTGCTGTACTGTTGTCGACCCAGGTC
ATGTTTCGAGATCAACCTGCACGTCGTGATGCAGTGCCAAGAGACGATAGCCCAGA
15 TGAATGAGTGGAGGGTTCATGAATGTCCACGTCGGTCTGGATGTCCGTGGCAAC
CTTGGTGTGGCTGATCGGAATCCACGATTGCAATGACAGCC (SEQ ID NO:52)

Translation:

MGKLTILVLVA AVLSTQVMFRDQPARRDAVPRDDSPDGMSGGFMNVPRRSGCPWQP
20 WCG (SEQ ID NO:53)

Toxin Sequence:

Ser-Gly-Cys-Xaa3-Xaa4-Gln-Xaa3-Xaa4-Cys-# (SEQ ID NO:54)

Name: Contryphan-Ar-1

Species: arenatus

Cloned: Yes

DNA Sequence:

ATGGGGAAACTGACAATACTGGTTCTTGTTGCTGCTGTACTGTTGTCGACCCAGGCC
ATGGTTCAAGATCAACCTGCAGGTCGAGATGCAGTTCCAAGAGACGATAACCCAGG
30 TGAACGAGTGGAAAGTTCGTGAATGCTCAACGTCAATATGGATGTCCGCCGGGTC
TTTGGTGTCACTGATCAGAATCCACGATTGCAATGACAGCC (SEQ ID NO:55)

Translation:

MGKLTILVLVA AVLSTQAMVQDQPAGRDAVPRDDNPGGTSGKFVNAQRQYGCPPGL
35 WCH (SEQ ID NO:56)

Toxin Sequence:

Xaa2-Xaa5-Gly-Cys-Xaa3-Xaa3-Gly-Leu-Xaa4-Cys-His-^ (SEQ ID NO:57)

Name: A10.1

45 **Species:** aurisiacus

Cloned: Yes

DNA Sequence:

ATGTTACACCGTGTCTTCTGTTGGTTGTCTTGGCAACCACTGTCGTTTCCATCCCTTCAG
 ATCGTGCACTCTGATGGCAGGAATGCCGCAGTCAACGAGAGAGCGCCTTGGCTGGTC
 5 CCTTCGACAATCACGACTTGCTGTGGATATAATCCGGGGACAATGTGCCCTCCTTGC
 AGGTGCGATAATACCTGTAAACCAAAAAAAAAAAAAAAAAAAAAA (SEQ ID NO:58)

Translation:

MFTVFLLVVLATTVVVSIPSDRASDGRNAAVNERAPWLVPSTITTCCGYNPGTMCPPCRC
 10 DNTC (SEQ ID NO:59)

Toxin Sequence:

Ala-Xaa3-Xaa4-Leu-Val-Xaa3-Ser-Thr-Ile-Thr-Thr-Cys-Cys-Gly-Xaa5-Asn-Xaa3-Gly-Thr-
 Met-Cys-Xaa3-Xaa3-Cys-Arg-Cys-Asp-Asn-Thr-Cys-^ (SEQ ID NO:60)

Name: Bn1.5
Species: bandanus
Cloned: Yes

DNA Sequence:

ATGCGCTGTCTCCAGTCTTGATCATTCTTCTGCTGCTGACTGCATCTGCACCTGGCG
 TTGATGTCCTACCGAAGACCGAAGATGATGTGCCCTGTGCATCTGTCTACGATAATA
 CAAAGAGTATCCTACGAGGACTTCTGGACAAACGTGCTTGCTGTGGCTACAAGCTTT
 25 GCTCACCATGTAAACCAGCATGAAGGATCC (SEQ ID NO:61)

Translation:

MRCLPVLIILLLLTAAPGVLDVLPKTEDDVPLSSVYDNTKSILRGLLDKRACCGYKLCSP
 30 C (SEQ ID NO:62)

Toxin Sequence:

Ala-Cys-Cys-Gly-Xaa5-Lys-Leu-Cys-Ser-Xaa3-Cys-^ (SEQ ID NO:63)

Name: Ca6.3
Species: caracteristicus
Cloned: Yes

DNA Sequence:

GGATCCATGAAACTGACGTGCGTGGTGATCATCGCCGCGCTGTTCTGACGGCCTGT
 CAGCTCAATACAGCTGATGACTCCAGAGATAAGCAGGAGTACCGTGCACTGAGGTT
 GAGAGACGGAATGCGGAATTTCAAAGGTTCCAAGCGCAACTGCGGGGAACAAGGT
 GAAGGTTGTGCTACTCGCCCATGCTGCTCTGGTCTGAGTTGCGTTGGCAGCCGTCCA
 GGAGGCCTGTGCCAGTACGGCTAATAGTCTGGCATCTGATATTTCCCTCTGCACTC
 45 TACCTTCTTTTGCCTGATGCATGTTTACTTGTGTGTGGTCATGAACCACTCAGTAGCT
 ACACCTCCGAAGGACGTGC (SEQ ID NO:64)

Translation:

MKLTCVVIIAALFLTACQLNTADDSRDKQEYRAVRLRDGMRNFKGSKRNCGEQGEGC
 ATRPCCSGLSCVGSRPGLCQYG (SEQ ID NO:65)

Toxin Sequence:

Asn-Cys-Gly-Xaa1-Gln-Gly-Xaa1-Gly-Cys-Ala-Thr-Arg-Xaa3-Cys-Cys-Ser-Gly-Leu-Ser-Cys-
 Val-Gly-Ser-Arg-Xaa3-Gly-Gly-Leu-Cys-Gln-Xaa5-# (SEQ ID NO:66)

Name: Ca8.1
Species: characteristicus
Cloned: Yes

DNA Sequence:

ATGATGTCGAAAATGGGAGCTATGTTTGTCTTTTGCTTCTTTTCATCCTGCCATCCA
 GCCAGCAGGAAGGAGATGTCCAGGCAAGAAAAACGCACCTGAAGAGAGGCTTCTA
 CGGTACTCTGGCAATGTCTACCAGAGGATGCTCTGGCACTTGCCATCGTCGTGAGGA
 CGGCAAGTGTCTGGGGTACTTGCGACTGCTCCGGATACAGCTATTGTCGCTGCGGTGA
 CGCTCACCATTTTTACCGAGGATGCACGTGTTCGTGTCAAGGTTGATTAATTGACTC
 TTTTAACTCGTTGAACGATTGAAAAAAAAAATTTTAGAGCAATATGTTTCGAGAAAA
 ACCGAAGAC (SEQ ID NO:67)

Translation:

MMSKMGAMFVLLLLFILPSSQQEGDVQARKTHLKRGFYGTLMSTRGCSGTCHRRRED
 GKCRGTCDCSGYSYCRCGDAHFFYRGCTCSCQG (SEQ ID NO:68)

Toxin Sequence:

Gly-Cys-Ser-Gly-Thr-Cys-His-Arg-Arg-Xaa1-Asp-Gly-Lys-Cys-Arg-Gly-Thr-Cys-Asp-Cys-
 Ser-Gly-Xaa5-Ser-Xaa5-Cys-Arg-Cys-Gly-Asp-Ala-His-His-Phe-Xaa5-Arg-Gly-Cys-Thr-Cys-
 Ser-Cys-Gln-# (SEQ ID NO:69)

Name: Ca8.2
Species: characteristicus
Cloned: Yes

DNA Sequence:

ATGATGTCGAAAATGGGAGCTATGTTTGTCTTTTGCTTCTTTTCATCCTGCCATCCA
 GCCAGCAGGAAGGAGATGTCCAGGCAAGAAAAACGCACCGGAAGAGCGGCTTCTA
 CGGTACTCTGGCAATGTCTGCCAGAGGATGCTCTGGCACTTGCCATCGTCGTGAGGA
 CGGCAAGTGTCTGGGGTACTTGCGACTGCTCCGGATACAGCTATTGTCGCTGCGGTGA
 CGCTCACCATTTTTACCGAGGATGCACGTGTACATGTTAAGGTTGATTAATTGACTC
 TTTTAACTCGTTGAACCGATTAAAAAAAAAATTAGACGAATATGTTTCGAGAAAACC
 GAAGAC (SEQ ID NO:70)

Translation:

MMSKMGAMFVLLLLFILPSSQQEGDVQARKTHRKSGFYGTLAMSARGCSGTCHRRED
GKCRGTCDCSGYSYCRCGDAHHFYRGCTCTC (SEQ ID NO:71)

Toxin Sequence:

5 Gly-Cys-Ser-Gly-Thr-Cys-His-Arg-Arg-Xaa1-Asp-Gly-Lys-Cys-Arg-Gly-Thr-Cys-Asp-Cys-
Ser-Gly-Xaa5-Ser-Xaa5-Cys-Arg-Cys-Gly-Asp-Ala-His-His-Phe-Xaa5-Arg-Gly-Cys-Thr-Cys-
Thr-Cys-^ (SEQ ID NO:72)

10 **Name:** Ca8.3
Species: characteristicus
Cloned: Yes

DNA Sequence:

15 ATGATGTCGAAAATGGGAGCTATGTTTGTCTTTTGCTTCTTTTCATCCTGCCATCCA
GCCAGCAGGAAGGAGATGTCCAGGCAAGAAAAACGCACCGGAAGAGCGGCTTCTA
CGGTACTCTGGCAATGTCTACCAGAGGATGCTCTGGCACTTGCCGTCGTCATCGGGA
CGGCAAGTGTCGGGGTACTTGCGACTGCTCCGGATACAGCTATTGTCGCTGCGGTGA
CGCTCACCATTTTTACCGAGGATGCACGTGTACATGTTAAGGTTGATTAATTCGATC
20 TTTTAACCTCGTTGAACGATTAAAAAAAATTTTAGACGAATATGTTCGAGAAAAA
CCGAAGAC (SEQ ID NO:73)

Translation:

25 MMSKMGAMFVLLLLFILPSSQQEGDVQARKTHRKSGFYGTLAMSTRGCSGTCRRHRD
GKCRGTCDCSGYSYCRCGDAHHFYRGCTCTC (SEQ ID NO:74)

Toxin Sequence:

30 Gly-Cys-Ser-Gly-Thr-Cys-Arg-Arg-His-Arg-Asp-Gly-Lys-Cys-Arg-Gly-Thr-Cys-Asp-Cys-Ser-
Gly-Xaa5-Ser-Xaa5-Cys-Arg-Cys-Gly-Asp-Ala-His-His-Phe-Xaa5-Arg-Gly-Cys-Thr-Cys-Thr-
Cys-^ (SEQ ID NO:75)

35 **Name:** Ca8.4
Species: characteristicus
Cloned: Yes

DNA Sequence:

40 ATGATGTCGAAAATGGGAGCTATGTTTGTCTTTTGCTTCTTTTCATCCTGCCATCCA
GCCAGCAGGAAGGAGATGTCCAGGCAAGAAAAACGCACCTGAAGAGAGGCTTCTA
CGGTACTCTGGCAATGTCTACCAGAGGATGCTCTGGCACTTGCCGTCGTCATCGGGA
CGGCAAGTGTCGGGGTACTTGCGACTGCTCCGGATACAGCTATTGTCGCTGCGGTGA
CGCTCACCATTTTTACCGAGGATGCACGTGTACATGTTAAGGTTGATTAATTGACTC
45 TTTTAACCTCGTTGAACGATTAAAAAAAATTTTAGAGCAATATGTTCGAGAAAAA
ACCGAAGAC (SEQ ID NO:76)

Translation:

MMSKMGAMFVLLLLFILPSSQQEGDVQARKTHLKRGFYGTLMSTRGCSGTCRRHRD
GKCRGTCDCSGYSYCRCGDAHHFYRGCTCTC (SEQ ID NO:77)

Toxin Sequence:

5 Gly-Cys-Ser-Gly-Thr-Cys-Arg-Arg-His-Arg-Asp-Gly-Lys-Cys-Arg-Gly-Thr-Cys-Asp-Cys-Ser-
Gly-Xaa5-Ser-Xaa5-Cys-Arg-Cys-Gly-Asp-Ala-His-His-Phe-Xaa5-Arg-Gly-Cys-Thr-Cys-Thr-
Cys-^ (SEQ ID NO:78)

10 **Name:** Ca8.5
Species: characteristicus
Cloned: Yes

DNA Sequence:

5 ATGATGTCGAAAATGGGAGCTATGTTTGTCTTTTGTCTTTTTCACCCTGCCATCCA
GCCAGCAGGAAGGAGATGTCCAGGCAAGAAAAACGCACCTGAAGAGAGGCTTCTA
CGGTACTCTGGCAATGTCTTCCAGAGGATGCTCTGGCACTTGCCATCGTCGTGAGGA
CGGCAAGTGTCGGGGTACTTGCGACTGCTCCGGATACAGCTATTGTCTGCTGCGGTGA
CGCTCACCATTTTTACCGAGGATGTACGTGTACATGTTAAGGTTGATTAATTGACTC
10 TTTTAACCTCGTTGAACGATTAAAAAAAATTTAGAGCAATATGTTTCGAGAAAACCG
AAGAC (SEQ ID NO:79)

Translation:

25 MMSKMGAMFVLLFLFTLPSSQQEGDVQARKTHLKRGFYGTLMSSRGCSGTCHRRERD
GKCRGTCDCSGYSYCRCGDAHHFYRGCTCTC (SEQ ID NO:80)

Toxin Sequence:

30 Gly-Cys-Ser-Gly-Thr-Cys-His-Arg-Arg-Xaa1-Asp-Gly-Lys-Cys-Arg-Gly-Thr-Cys-Asp-Cys-
Ser-Gly-Xaa5-Ser-Xaa5-Cys-Arg-Cys-Gly-Asp-Ala-His-His-Phe-Xaa5-Arg-Gly-Cys-Thr-Cys-
Thr-Cys-^ (SEQ ID NO:81)

35 **Name:** Ca8.6
Species: characteristicus
Cloned: Yes

DNA Sequence:

40 ATGATGTCGAAAATGGGAGCTATGTTTGTCTTTTGTCTTTTTCATCCTGCCATCCA
GCCAGCAGGAAGGAGATGTCCAGGCAAGAAAAACGCACCTGAAGAGCGGCTTCTA
CGGTACTCTGGCAATGTCTGCCAGAGGATGCTCTGGCACTTGCCATCGTCGTCAAAA
CGGCGAGTGTCAGGGTACTTGCGACTGCGACGGACACGACCATTGTGACTGCGGTG
ACACTCTCGGTACTTACTCAGGATGCGTGTGTATATGTTAAGGTTGATTAATTGACT
CTTTTAACCTCGTTGAACGATTAAAAAAAATTTAGAGCAATATGTTTCGAGAAAAACCG
45 AAGAC (SEQ ID NO:82)

Translation:

MMSKMGAMFVLLLLFILPSSQQEGDVQARKTHLKSGFYGTLAMSARGCSGTCHRRQN
GECQGTCDGHDHCDGDTLGTYSGCVCIC (SEQ ID NO:83)

Toxin Sequence:

5 Gly-Cys-Ser-Gly-Thr-Cys-His-Arg-Arg-Gln-Asn-Gly-Xaa1-Cys-Gln-Gly-Thr-Cys-Asp-Cys-
Asp-Gly-His-Asp-His-Cys-Asp-Cys-Gly-Asp-Thr-Leu-Gly-Thr-Xaa5-Ser-Gly-Cys-Val-Cys-Ile-
Cys-^ (SEQ ID NO:84)

10 **Name:** Ca9.1
Species: characteristicus
Cloned: Yes

DNA Sequence:

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MHLSLARS AVLMLLLFALDNFVGVQPGQITRDVDNRRNLQSRWKPRSLFKSLHKRAS
CGGTCTESADCPSTCSTCLHAQCE (SEQ ID NO:89)

Toxin Sequence:

5 Ser-Cys-Gly-Gly-Thr-Cys-Thr-Xaa1-Ser-Ala-Asp-Cys-Xaa3-Ser-Thr-Cys-Ser-Thr-Cys-Leu-
His-Ala-Gln-Cys-Xaa1-^ (SEQ ID NO:90)

Name: Cr10.2
Species: circumcised
Cloned: Yes

DNA Sequence:

tgtgtgtgtgtgttctgggtccaGCATTTGATGGCAGGAATGCCGCAGTCAACGAGAGAGCGCCT
5 TGGACGGTTCGTTTTGTCCACCACGAATTGCTGCGGTTATAATACGATGGAATTCTGC
CCTGCTTGCATGTGCACTTATTCCTGTCCAAAAAAGAAAAAACCAGGAAAAGGCCG
CAGAAACAACCTGATGCTCCAGGACCCTCTGAACCACGACGT (SEQ ID NO:91)

Translation:

20 FDGRNAAVNERAPWTVVLSTTNCCGYNTMEFCPACMCTYSCPKKKKPGKGRRNN
(SEQ ID NO:92)

Toxin Sequence:

25 Ala-Xaa3-Xaa4-Thr-Val-Val-Leu-Ser-Thr-Thr-Asn-Cys-Cys-Gly-Xaa5-Asn-Thr-Met-Xaa1-
Phe-Cys-Xaa3-Ala-Cys-Met-Cys-Thr-Xaa5-Ser-Cys-Xaa3-Lys-Lys-Lys-Lys-Xaa3-Gly-Lys-
Gly-Arg-Arg-Asn-Asn-^ (SEQ ID NO:93)

Name: Cn9.1
Species: consors
Cloned: Yes

DNA Sequence:

Translation:

35 GIFVGVQPEQITRDVDKGYSTDDGHDLLSLKQISLRAC TGSCNSDSECYNFCDCIGTRC
EAQK (SEQ ID NO:94)

Toxin Sequence:

40 Ala-Cys-Thr-Gly-Ser-Cys-Asn-Ser-Asp-Ser-Xaa1-Cys-Xaa5-Asn-Phe-Cys-Asp-Cys-Ile-Gly-
Thr-Arg-Cys-Xaa1-Ala-Gln-Lys-^ (SEQ ID NO:95)

Name: De6.1
Species: delessertii
Isolated: Yes

Toxin Sequence:

Ala-Cys-Lys-Xaa3-Lys-Asn-Asn-Leu-Cys-Ala-Ile-Thr-Xaa1-Met-Ala-Xaa1-Cys-Cys-Ser-Gly-Phe-Cys-Leu-Ile-Xaa5-Arg-Cys-^ (SEQ ID NO:96)

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Name: Bromosleeper-Di1
Species: distans
Cloned: Yes

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DNA Sequence:

GACAGGATTGAACAAAATTCAGGATGTCAGGATTGGGAATCATGGTGCTAACCCTT
 CTACTTCTTGTGCCCATGGCAACCAGTCAACAGGATGGAGGAGAGAAGCAGGCGAT
 GCAAAGGGACGCAATCAACGTCGCACCAGGAACATCAATCACTCGGAGAAATGTA
 GATCAGGAGTGCATTGACGCCTGTCAGCTGGAGGACAAGAATTGCTGTGGCAGAAC
 AGATGGAGAACCCAGATGTGCGAAAATCTGCCTCGGATAATTTCTGTACGCTGTCTC
 ATTCATTATTTTCATCCGTACGAGTGTAACGAGACCTATTAGAAAGTCGAAGGTTGT
 GCGTAATTTGATAAGCATTGTTTGCTGGGACGAACGGA (SEQ ID NO:97)

Translation:

MSGLGIMVLTLTLLVPMATSQQDGGEKQAMQRDAINVAPGTSITRRNVDQECIDACQL
 EDKNCCGRTDGEPRCAKICLG (SEQ ID NO:98)

Toxin Sequence:

Asn-Val-Asp-Gln-Xaa1-Cys-Ile-Asp-Ala-Cys-Gln-Leu-Xaa1-Asp-Lys-Asn-Cys-Cys-Gly-Arg-Thr-Asp-Gly-Xaa1-Xaa3-Arg-Cys-Ala-Lys-Ile-Cys-Leu-# (SEQ ID NO:99)

Name: Bromosleeper-Di2
Species: distans
Cloned: Yes

DNA Sequence:

GACAGGATTGAACAAAATTCAGGATGTCAGGATTGGGAATCATGGTGCTAACCCTT
 CTACTTCTTGTGCCCATGGCAACCAGTCAACAGGATGGAGGAGAGAAGCAGGCGAT
 GCAAAGGGACGCAATCAACGTCGCACCAGGAACATCAATCACTCGGACAGAAACA
 GATCAGGAGTGCATTGACATCTGTAAGCAGGAGGACAAGAAATGCTGCGGCAGATC
 AAATGGAGAACCCACATGTGCGAAAATCTGCCTCGGATAATTTCTGTACGCTGTCTC
 GTTCATTATTTTCGTCAGTACGAGTTTAAACGAGACCTATTAGAAAGTCGAAGGTTTCG
 TGCTTAATTTGATAAGCATTGTTTGCTGGGATGAACGGA (SEQ ID NO:100)

Translation:

MSGLGIMVLTLTLLVPMATSQQDGGEKQAMQRDAINVAPGTSITRTETDQECIDICKQE
 DKKCCGRSNGEPTCAKICLG (SEQ ID NO:101)

Toxin Sequence:

Xaa1-Thr-Asp-Gln-Xaa1-Cys-Ile-Asp-Ile-Cys-Lys-Gln-Xaa1-Asp-Lys-Lys-Cys-Cys-Gly-Arg-Ser-Asn-Gly-Xaa1-Xaa3-Thr-Cys-Ala-Lys-Ile-Cys-Leu-# (SEQ ID NO:102)

Name: Bromosleeper-Di3
Species: distans
Cloned: Yes

DNA Sequence:

GACAGGATTGAACAAAATTCAGGATGTCAGGATTGGGAATCATGGTGCTAACCCTT
CTACTTCTTGTGCCCATGGCAACCAGTCAACAGGATGGAGGAGAGAAGCAGGCGAT
GCAAAGGGACGCAATCAACGTCGCACCAGGAACATCAATCACTCGGAGAGAAACA
GATCAGGAGTGCAATTGACACCTGTGAGCAGGAGGACAAGAAATGCTGCGGCAGAA
CAAATGGAGAACCCGTATGTGCGAAAATCTGCTTCGGATAATTTCTGTACGCTGTCT
CATTATAATTTATCAGTACGAGTTTAAACGAGACCTATTAGAAAGTCGAAGGTTC
GTGCTTAATTTGATAAGCATTGTTTGCTGGGATGAACGGA (SEQ ID NO:103)

Translation:

MSGLGIMVL TLLL VPMATSQQDGGEKQAMQRDAINVAPGTSITRRETDQECIDTCEQE
DKKCCGRTNGEPVCAKICFG (SEQ ID NO:104)

Toxin Sequence:

Xaa1-Thr-Asp-Gln-Xaa1-Cys-Ile-Asp-Thr-Cys-Xaa1-Gln-Xaa1-Asp-Lys-Lys-Cys-Cys-Gly-
Arg-Thr-Asn-Gly-Xaa1-Xaa3-Val-Cys-Ala-Lys-Ile-Cys-Phe-# (SEQ ID NO:105)

Name: α A-EIVB
Species: ermineus
Isolated: Yes
Cloned: Yes

DNA Sequence:

ATGTTACACGTGTTTCTGTTGGTTGTCTTGGCAACCACTGTCGTTTCCTTCACTTCAG
ATCGTGCATCGGATGACAGGAATACCAACGACAAAGCATCTCGCCTGCTCTCTCAC
GTTGTCAGGGGATGCTGTGGTAAGTATCCCAATGCTGCCTGTCATCCTTGCGGTTGT
ACAGTGGGTAGGCCACCGTATTGTGACAGACCCAGTGGTGGAGGACGCTGATGCTC
CAGGACCCTCTGAACCACGACGT (SEQ ID NO:106)

Translation:

MFTVFLLVVLATTVVSFTSDRASDDRNTNDKASRLLSHVVRGCCGKYPNAACHPCGCT
VGRPPYCDRPSGGGR (SEQ ID NO:107)

Toxin Sequence:

Gly-Cys-Cys-Gly-Lys-Xaa5-Xaa3-Asn-Ala-Ala-Cys-His-Xaa3-Cys-Gly-Cys-Thr-Val-Gly-Arg-
Xaa3-Xaa3-Xaa5-Cys-Asp-Arg-Xaa3-Ser-Gly-Gly-# (SEQ ID NO:108)

Name: Ge3.1
Species: generalis
Cloned: Yes

5 **DNA Sequence:**

GGATCCATGATGTCTAAACTGGGAGTCTTGTTGACCATCTGTCTGGTTCTGTTTCCCC
 TTACTGCTCTTCCACTGGATGGAGAACAACCTGTAGACCGACATGCCGAGCATATGC
 AGGATGACAATTCAGCTGCACAGAACCCCTGGGTTATTGCCATCAGACAGTGTTGC
 ACGTTCTGCAACTTTGGATGCCAGCCTTGTTGCGTCCCCTGATAACGTGTTGATGAC
 10 CAACTTTCTCGAG (SEQ ID NO:109)

Translation:

GSMMSKLGVLLTICLVLFPLTALPLDGEQPVDRHAEHMQDDNSAAQNPWVIAIRQCCT
 FCNFGCQPCCVP (SEQ ID NO:110)

Toxin Sequence:

Xaa2-Cys-Cys-Thr-Phe-Cys-Asn-Phe-Gly-Cys-Gln-Xaa3-Cys-Cys-Val-Xaa3-^ (SEQ ID
 NO:111)

Name: C. geographus GS-A
Species: geographus
Cloned: Yes

25 **DNA Sequence:**

GCAAGATCATCAGCAGAATGAACCTGACGTGCGTGTTGATCATCGCCGTGCTGTTTC
 TGACGGCCTGCCAGCTCATTGCAGCTGATGACTCCAGAGATAACCAGAAGCACCGT
 GCAGTGAGGATGAGAGACGCATTGAAGAATTTCAAAGATTCCAGGGCGTGCTCCGG
 TAGAGGTTCTAGATGTCCTCCCCAATGCTGCATGGGTTTGACGTGCGGTCGTGAGTA
 30 TCCACCCAGATGCGGTTGATATACGGTGAACAACTGATATTTCCCCTCTGTGCTCTA
 CCCTCTTTTGCCTGATTCACCCACACCTATGTGTGGTCATGAACCACTCAGTACCTA
 CACCTCTGGTGGCTTCAGAGGACGTATATTAATAAAATAAAACCACATTGCAATGAAAA
 AAAAAAAAA (SEQ ID NO:112)

35 **Translation:**

MNLTCVLIHAVLFLTACQLIAADDSRDNQKHRAVRMRDALKNFKDSRACSGRGSRCPP
 QCCMGLTCGREYPPRCG (SEQ ID NO:113)

Toxin Sequence:

40 Ala-Cys-Ser-Gly-Arg-Gly-Ser-Arg-Cys-Xaa3-Xaa3-Gln-Cys-Cys-Met-Gly-Leu-Thr-Cys-Gly-
 Arg-Xaa1-Xaa5-Xaa3-Xaa3-Arg-Cys-# (SEQ ID NO:114)

45 **Name:** Conopressin-G
Species: geographus
Isolated: Yes

Toxin Sequence:

Cys-Phe-Ile-Arg-Asn-Cys-Xaa3-Lys-Gly-# (SEQ ID NO:115)

5 **Name:** EST66
Species: geographus
Cloned: Yes

DNA Sequence:

10 TGCTGCCCCGAGTAGCAAAGAGGATTCCCTGAACTGCATTGAGACCATGGCGACCAC
 GGCCACGTGCATGAAGTCCAACAAGGGGGAGATCTACTCCTATGCGTGCGGCTACT
 GCGGCAAGAAGAAGGAGAGCTGTTTCGGCGACAAAAAGCCAGTGACTGACTACCA
 GTGCCAGACGCGGAACATTCCCAACCCCTGCGGCGGCGCTGCTCTCTGAAGGCACC
 AACAGCACCAACAGCACGATCTCCTGTGTTTCGTCACCTGCATTTATGACGTCAAAAC
 15 CACGTCATGCATGATGACGACGATCTCGGCTATGGCATGTATTGAAGAATGGAAAT
 AAACCTAGTTTTTCAGCTGAAAAAA (SEQ ID NO:116)

Translation:

20 CCPSSKEDSLNCIETMATTATCMKSNKGEIYSYACGYCGKKKESCFGDKKPVTDYQCQ
 TRNIPNCGGAAL (SEQ ID NO:117)

Toxin Sequence:

25 Cys-Cys-Xaa3-Ser-Ser-Lys-Xaa1-Asp-Ser-Leu-Asn-Cys-Ile-Xaa1-Thr-Met-Ala-Thr-Thr-Ala-
 Thr-Cys-Met-Lys-Ser-Asn-Lys-Gly-Xaa1-Ile-Xaa5-Ser-Xaa5-Ala-Cys-Gly-Xaa5-Cys-Gly-Lys-
 30 Lys-Lys-Xaa1-Ser-Cys-Phe-Gly-Asp-Lys-Lys-Xaa3-Val-Thr-Asp-Xaa5-Gln-Cys-Gln-Thr-Arg-
 Asn-Ile-Xaa3-Asn-Xaa3-Cys-Gly-Gly-Ala-Ala-Leu-^ (SEQ ID NO:118)

30 **Name:** EST87
Species: geographus
Cloned: Yes

DNA Sequence:

35 CGGGCGCTGCATTCCGGACGTGAAACAGCATCGCCAGCAAGTGGGCATAGTGCAAG
 ACACtCAGAACAAtGACGCACAtAGTCTGANAAAATAACCATGGGTATGCGGATGAN
 GTTTAGTGTGTTTCNGCAGGTTGTCNTGGGNACCACTGTCGTTTCCTTCACNTCACGT
 CGTGGTCCAAAATCTCGTCGCGGGGAACCTATTCCGACCACTGTAATCAACTACGG
 GGAGTGCTGTAAGGATCCATCCTGTTGGGTGAAGGTGAAGGATTTCCAGTGTCTGG
 AGCAAGTCTCCCAACTGAACCACGACATGTCGCCCTCTGCCTGACCTGCTTCACGT
 40 TCCGTCTCTTTCTGCCACTAGAACTCAACAACTCGATCCAACAGACTCCTACTTTAC
 CTCCGTATTCTGAAACTACTTGGATTTGATTGTCTTTAATATCTACTCACACTTGCTG
 TTATTACATCATCCAAAATTTAACAAGAACATGAAAGGTGTCTGTTCAAACAAAATC
 AGGCAATGACAANGGGGAAAGTCTCCANTCTATCTGAAAAGTGTACCTGTCACT
 CTCTTAACCAGGTTTANAAGTANTACCACTANAGCTGTTGTNCCACATCANGATCA
 45 GNCCAATTTGTANNGTTTCCTTTGCAAAACTTTTGCTGAAATCTTGAAAAGAAAC
 GCTCACAATGTTGGGAAGTGCTTTTATTANCTGACAANNTGNCANCATGTTCCNTT
 TCANTAANTCTNAAATGNAAACCTCTGTT (SEQ ID NO:119)

Translation:

MGMRMMFVFLQVVLGTTVVVSFTSRRGPKSRRGEPIPTTVINYGECCKDPSCWVKVKD
FQCPGASPPN (SEQ ID NO:120)

Toxin Sequence:

Gly-Xaa1-Xaa3-Ile-Xaa3-Thr-Thr-Val-Ile-Asn-Xaa5-Gly-Xaa1-Cys-Cys-Lys-Asp-Xaa3-Ser-
Cys-Xaa4-Val-Lys-Val-Lys-Asp-Phe-Gln-Cys-Xaa3-Gly-Ala-Ser-Xaa3-Xaa3-Asn-^ (SEQ ID
NO:121)

Name: G12.1

Species: geographus

Cloned: Yes

DNA Sequence:

AGCCTTGATACAGAGCTGGTATCTGCTGTTAATACTTGAAAGAACAAGTGCTGTGA
GCCTTCATCTCTCTCTGACTTTAGTTTGGGTCCTGGAGAAAACCTTGACGGGCAGTA
TGAAAATTTACCTGTGTCTTGCTTTTGTTCTGCTCCTGGCTTCTACCATAGTTGATT
AGGGCTTCTTGATAAAATTGAGACTATAAGAACTGGAAACGCGATGACAGCTATT
GTGATGGATGCCTATGCACCATATTAAGAAAGAGACTTGCACATCGACTATGAGC
TGCAGGGGAACATGCCGAAAAGAGTGGCCATGTTGGGAAGAAGACTGCTACTGTAC
TGAAATCCAAGGTGGAGCTTGCCTCACACCCTCAGAATGCAAACCTGGAGAGTGTT
GAGGATTGGAGTGGCCAGTTCCAGCACATACAGCACCATGGTGCCCTGGACAATCG
TCTATTGAATTGAATATGCCTGTGGCAGGAATCTGTCCTACAAAATAAAAAAATCAT
AAGTTAAAAAA (SEQ ID NO:122)

Translation:

MKIYLCCLAFVLLLASTIVDSGLLDKIETIRNWKRDDSYCDGCLCTILKKETCTSTMSCR
GTCRKEWPCWEEDCYCTEIQQGACVTPSECKPGEC (SEQ ID NO:123)

Toxin Sequence:

Asp-Asp-Ser-Xaa5-Cys-Asp-Gly-Cys-Leu-Cys-Thr-Ile-Leu-Lys-Lys-Xaa1-Thr-Cys-Thr-Ser-
Thr-Met-Ser-Cys-Arg-Gly-Thr-Cys-Arg-Lys-Xaa1-Xaa4-Xaa3-Cys-Xaa4-Xaa1-Xaa1-Asp-Cys-
Xaa5-Cys-Thr-Xaa1-Ile-Gln-Gly-Gly-Ala-Cys-Val-Thr-Xaa3-Ser-Xaa1-Cys-Lys-Xaa3-Gly-
Xaa1-Cys-^ (SEQ ID NO:124)

Name: G12.2

Species: geographus

Cloned: Yes

DNA Sequence:

AACGTTGACGGGCAGTATGAACATTTACCTGTGTCTTGCTTTTCTTCTGTTCCCTGCCT
TCTACCATAGTTGATTTCAGGGCTTCTTGATAAAATTGAGACAATAAGGAATTGGAGA
CGTGATGAAAGCAAGTGTGATCGATGCAATTGCGCCGAATTAAGATCATCCAGATG
CACACAAGCTATCTTCTGCCTTACACCGGAGTTATGCACACCGAGCATCTCATGTCC

GACAGGTGAATGCCGCTGTACTAAGTTCCATCAGTCAAGATGCACTAGATTTCGTAG
AATGCGTACCTAATAAGTGTAGAGACGCATAGAGGCCAGTTCCAGCACATACAGCA
CCATGATGCCCTGGACAATCGTGTTGTTGGATTGAATATGCCCCGTGGCAGGAATCTG
TCCTACAAAAAA (SEQ ID NO:125)

5

Translation:

MNIYLCLAFLLFLPSTIVDSGLLDKIETIRNWRRDESKCDRCNCAELRSSRCTQAIFCLTP
ELCTPSISCTGECRCKTFHQSRCTRFVECVPNKCRDA (SEQ ID NO:126)

10

Toxin Sequence:

Asp-Xaa1-Ser-Lys-Cys-Asp-Arg-Cys-Asn-Cys-Ala-Xaa1-Leu-Arg-Ser-Ser-Arg-Cys-Thr-Gln-
Ala-Ile-Phe-Cys-Leu-Thr-Xaa3-Xaa1-Leu-Cys-Thr-Xaa3-Ser-Ile-Ser-Cys-Xaa3-Thr-Gly-Xaa1-
Cys-Arg-Cys-Thr-Lys-Phe-His-Gln-Ser-Arg-Cys-Thr-Arg-Phe-Val-Xaa1-Cys-Val-Xaa3-Asn-
Lys-Cys-Arg-Asp-Ala-^ (SEQ ID NO:127)

Name: Scratching,convulsion

Species: geographus

Isolated: Yes

Toxin Sequence:

Lys-Phe-Leu-Ser-Gly-Gly-Phe-Lys-Xaa1-Ile-Val-Cys-His-Arg-Xaa5-Cys-Ala-Lys-Gly-Ile-Ala-
Lys-Xaa1-Phe-Cys-Asn-Cys-Xaa3-Asp-# (SEQ ID NO:128)

Name: Contryphan-Im

Species: imperialis

Isolated: Yes

30

Toxin Sequence:

Xaa2-Cys-Gly-Gln-Ala-Xaa4-Cys-# (SEQ ID NO:129)

Name: Im9.1

35

Species: imperialis

Cloned: Yes

DNA Sequence:

GTAAAAATGCATCTGTCACTGGCAAGCTCAGCTGCTTTGATGTTGCTTCTGCTTTTTG
CCTTGGGCAACTTCGTTGGGGTCCAGCCAGGACAAATAAGAGATCTGAACAAAGGA
CAGCTCAAGGACAACCGCCGTAACCTGCAATCGCAGAGGAAACAAATGAGTCTCCT
CAAGTCACTTCATGATCGAAATGGGTGTAACGGCAACACGTGTTCCAATAGCCCCCT
GCCCTAACAACTGTTATTGCGATACTGAGGACGACTGCCACCCTGACAGGCGTGAA
CATAGAGATTAGAGAGTTTCTTGTCAACATGATGTGCGACCACACCTCTGCTCTG
CAGTGTGTACATCGACCAGTCGACGCATCTGTTATTTCTTTGTCTGTTGGATTGTACA
TCGACCAGTCCACGCATCTGTTATTTCTTTGTCTGTTTGATTGTTTTCGTGTGTTTCAT

AACACACAGAGCCTTTCTATTATCTGTATTGCAATACACTTTGCCTGATAACCAGAA
AGTCCAGTGCT (SEQ ID NO:130)

Translation:

5 MHLSLASSAALMLLLFALGNFVGVQPGQIRDLNKGQLKDNRRNLQSQRKQMSLLKSL
HDRNGCNGNTCSNSPCPNNCYCDTEDDCHPDRREH (SEQ ID NO:131)

Toxin Sequence:

10 Asn-Gly-Cys-Asn-Gly-Asn-Thr-Cys-Ser-Asn-Ser-Xaa3-Cys-Xaa3-Asn-Asn-Cys-Xaa5-Cys-
Asp-Thr-Xaa1-Asp-Asp-Cys-His-Xaa3-Asp-Arg-Arg-Xaa1-His-^ (SEQ ID NO:132)

Name: La8.1
Species: laterculatus
Cloned: Yes

DNA Sequence:

ATGATGTCGAAAAATGGGAGCTATGTTTGTCTTTTGTCTTTTACCCTGGCATCCA
GCCAGCAGGAAGGAGATGTCCAGGCAAGGAAAACACACCCGAAGAGAGAGTTCCA
TCGTATTCTGCTAAGGCCTGACAGACAGTCCGAAACGGCTTGTAGGTCTGCTCGGAA
GCTACCAATGTATGGGTAAATGCCAACTCGGGGTTTATTCTGGTGTGAATGCATT
ATAACCGAGGTAGTCAGAAGTCTGGATGCGCGTGTAGGTGTCAAAAGTGATTAATT
GACTCATTTAACTCGTTGAACGATTTAAAAAATCCAGAGCAATATGTTTCGAGAAAA
ACCGAAGACGAC (SEQ ID NO:133)

Translation:

MMSKMGAMFVLLLLFTLASSQQEGDVQARKTHPKREFHRILLRPDRQSETACRSLGSY
QCMGKCQLGVHSWCECIYNRGSQKSGCACRCQK (SEQ ID NO:134)

Toxin Sequence:

30 Xaa2-Ser-Xaa1-Thr-Ala-Cys-Arg-Ser-Leu-Gly-Ser-Xaa5-Gln-Cys-Met-Gly-Lys-Cys-Gln-Leu-
Gly-Val-His-Ser-Xaa4-Cys-Xaa1-Cys-Ile-Xaa5-Asn-Arg-Gly-Ser-Gln-Lys-Ser-Gly-Cys-Ala-
Cys-Arg-Cys-Gln-Lys-^ (SEQ ID NO:135)

Name: Lv6.2
Species: lividus
Cloned: Yes

DNA Sequence:

GGATCCATGAAACTGACGTGTGTGGTGATCATCGCCGTGCTGTTCTGACGGCCAGT
CAGCTCATTACAGCTGATTACTCCAGAGATAAGCAGGAGTATCGTGACAGAGAGGCT
GAGAGACGCAATGGGGAAATTCAAAGGTTCCAGGTCGTGCGGACATAGTGGTGCAG
GTTGTTATACTCGCCCTTGCTGCCCTGGTCTGCATTGCTCTGGCGGCCAAGCTGGAG
45 GCCTGTGCGTGTAAAGTAATAATCTGGCGTCTGATATTTCCAGTCTGTGCTCTACC
CTCTTTTGCCTGAGTCATCCATACCTGTGCTCGAG (SEQ ID NO:136)

Translation:

MKLTCVVIIAVLFLTASQLITADYSRDKQEYRAERLRDAMGKFKGSRSCGHSGAGCYT
RPCCPGLHCSGGQAGGLCV (SEQ ID NO:137)

5

Toxin Sequence:

Ser-Cys-Gly-His-Ser-Gly-Ala-Gly-Cys-Xaa5-Thr-Arg-Xaa3-Cys-Cys-Xaa3-Gly-Leu-His-Cys-
Ser-Gly-Gly-Gln-Ala-Gly-Gly-Leu-Cys-Val-^ (SEQ ID NO:138)

10

Name: Lv6.3
Species: lividus
Cloned: Yes

15

DNA Sequence:

GGATCCATGAAACTGACGTGTGTGGTGATCATATCCGTGCTGTTTCCTGACGGCCAGT
GAGTTCCTTACAGCTGATTACTCCAGAGATAAGCGGCAGTACCGTGCTGTGAGGTTG
AGAGACGCAATGCGGAATTTCAAAGGTACCAGGGACTGCGGGGAATCAGGTCAAG
GTTGCTATAGTGTACGTCCTTGCTGCCCTGGTCTGATTTGCAAAGGCACCGGTGGTG
GAGGCCTGTGCCGGCCCTCTGGCATCTGATATCTCCCCTCTGTGCTCCACCCTCTTTT
GCCTGAGTCATCCATACCTGTGCTCGAG (SEQ ID NO:139)

20

25

Translation:

MKLTCVVIIISVLFLTASEFLTADYSRDKRQYRAVRLRDAMRNFKGTRDCGESGQGCYS
VRPCCPGLICKGTGGGGLCRPSGI (SEQ ID NO:140)

30

Toxin Sequence:

Asp-Cys-Gly-Xaa1-Ser-Gly-Gln-Gly-Cys-Xaa5-Ser-Val-Arg-Xaa3-Cys-Cys-Xaa3-Gly-Leu-Ile-
Cys-Lys-Gly-Thr-Gly-Gly-Gly-Gly-Leu-Cys-Arg-Xaa3-Ser-Gly-Ile-^ (SEQ ID NO:141)

35

Name: Convulsant
Species: magus
Isolated: Yes

40

Toxin Sequence:

Val-Xaa5-Xaa1-Thr-His-Xaa3-^ (SEQ ID NO:142)

45

Name: MAG-1
Species: magus
Isolated: Yes

Toxin Sequence:

Arg-Xaa3-Lys-Asn-Ser-Xaa4-^ (SEQ ID NO:143)

50

Name: MAG-2
Species: magus
Isolated: Yes

5 **Toxin Sequence:**
 Ala-Arg-Xaa3-Lys-Asn-Ser-Xaa4-? (SEQ ID NO:144)

10 **Name:** MAG-3
Species: magus
Isolated: Yes

Toxin Sequence:

15 Arg-Xaa3-Lys-Asn-Ser-Xaa4-^ (SEQ ID NO:145)

Name: Mi6.2
Species: miles
Cloned: Yes

DNA Sequence:

GGATCCATGAAACTGACGTGCGTGGTGATCGTCGCCGTGCTGTTCCCTGACGGCCTGT
 CAACTCATTACTGCTGCGAATTACGCCAGAGATGAACAGGAGTACCCCGCTGTGAG
 GTCGAGCGACGTGATGCAGGATTCCGAAGACTTGACGTTGACCAAGAAATGCACGG
 ACGATTCTCAGTTCTGTAACCCCTTCGAATCATGACTGCTGCAGTGGGAAGTGTATCG
 ACGAAGGAGACAACGGCATATGCGCTATAGTCCCTGAAAACTCTTAACAATGTATA
 CTGACATTTCCCCCTCTGTGCTCCGCCGTCCGTGGCCTGACTCGTCCATCCTTGGGCG
 TGGTCATGAACCGCTCGGTT (SEQ ID NO:146)

Translation:

MKLTCVVIVAVLFLTACQLITAANYARDEQEYPAVRSSDVMQDSEDLTLLTKKCTDDSQ
 FCNPSNHDCCSGKCIDEGDNGICAIVPENS (SEQ ID NO:147)

35 **Toxin Sequence:**
 Cys-Thr-Asp-Asp-Ser-Gln-Phe-Cys-Asn-Xaa3-Ser-Asn-His-Asp-Cys-Cys-Ser-Gly-Lys-Cys-Ile-
 Asp-Xaa1-Gly-Asp-Asn-Gly-Ile-Cys-Ala-Ile-Val-Xaa3-Xaa1-Asn-Ser-^ (SEQ ID NO:148)

40 **Name:** Mi6.3
Species: miles
Cloned: Yes

DNA Sequence:

45 GGATCCATGAAACTGACGTGTGTGGTGATCGTCGCCGTGCTGTTCCCTGACGGCCTGT
 CAACTCATTACTGCTGCGAATTACGCCAGAGATGAACAGGAGTACCCTGCTGTGAG
 GTCGAGCGACGTGATGCAGGATTCCGAAGACCTGACGTTGACCAAGAAATGCACGG

AGGATTCTCAGTTCTGTAACCCTTCGAATCATGACTGCTGCAGTGGGAAGTGTATCG
ACGAAGGAGACAACGGCATATGCGCTATAGTCCCTGAAACTCTTAACAATGTATA
CTGACATTTCCCCCTCTGTGCTCCGCCGTCCGTGGCCTGACTCGTCCATCCTTGGGCG
TGGTCATGAACCGCTCG (SEQ ID NO:149)

5

Translation:

MKLTCVVIVAVLFLTACQLITAANYARDEQEYPAVRSSDVMQDSEDLTLKKCTEDSQ
FCNPSNHDCCSGKCIDEGDNGICAIVPENS (SEQ ID NO:150)

10

Toxin Sequence:

Cys-Thr-Xaa1-Asp-Ser-Gln-Phe-Cys-Asn-Xaa3-Ser-Asn-His-Asp-Cys-Cys-Ser-Gly-Lys-Cys-
Ile-Asp-Xaa1-Gly-Asp-Asn-Gly-Ile-Cys-Ala-Ile-Val-Xaa3-Xaa1-Asn-Ser-^ (SEQ ID NO:151)

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Name: Mf6.1
Species: miliaris
Cloned: Yes

DNA Sequence:

GGATCCATGAACTGACGTGTGTGGTGATCATCGCCGTGCTGTTCTTGACGGCCTGTC
AACTCACTACAGCTGTGACTTCCTCCAGAGGTCAACAGAAGCATCGTGCTCTGAGGT
CAACTGACAAAACTCCAGGATGACCAAGCGTTGCACGCCTCCAGGTGGACTCTGT
TACCATGCTTATCCCTGCTGCAGCAAGACTTGCAATCTCGATACCAGCCAATGTGAG
CCTAGGTGGTCATGAACCACTCAATACCCTCTCCTCTGGAGGCTTCAGAGGAACTAC
ATTGAAATAAAACCGCATTGCAACGAAAAAAAAAAAAAAAAAAAA (SEQ ID NO:152)

Translation:

LTCVVIIAVLFLTACQLTTAVTSSRGQQKHRALRSTDKNSRMTKRCTPPGGLCYHAYPC
CSKTCNLDTSQCEPRWS (SEQ ID NO:153)

30

Toxin Sequence:

Cys-Thr-Xaa3-Xaa3-Gly-Gly-Leu-Cys-Xaa5-His-Ala-Xaa5-Xaa3-Cys-Cys-Ser-Lys-Thr-Cys-
Asn-Leu-Asp-Thr-Ser-Gln-Cys-Xaa1-Xaa3-Arg-Xaa4-Ser-^ (SEQ ID NO:154)

35

Name: Mn10.3
Species: monachus
Cloned: Yes

40

DNA Sequence:

tgtgtgtgtgtgttctgggtccaGCATCTGATGTCAGGAATGCCGCAGTCCACGAAAGACAGAAG
GATCTGGTCGTTACGGCCACCACGACTTGCTGTGGTTATAATCCGATGACAATGTGC
CCTCCTTGATGTGCACTAATACCTGCAAAAAAAGTGGCTGATGCTCCAGGACCCTC
TGAACCACGACGT (SEQ ID NO:155)

45

Translation:

SDVRNAAVHERQKDLVVTATTTCCGYNPMTMCPPCMCTNTCKKSG (SEQ ID NO:156)

Toxin Sequence:

Xaa2-Lys-Asp-Leu-Val-Val-Thr-Ala-Thr-Thr-Thr-Cys-Cys-Gly-Xaa5-Asn-Xaa3-Met-Thr-Met-Cys-Xaa3-Xaa3-Cys-Met-Cys-Thr-Asn-Thr-Cys-Lys-Lys-Ser-# (SEQ ID NO:157)

Name: Mn8.1
Species: monachus
Cloned: Yes

DNA Sequence:

ATGATGTCGAAAATGGGAGCTATGTTTGTCTTTTGTCTTTTACCCCTGGCATCCA
GCCAGCAGGAAGGAGATGTCCAGGCAAGGAAAACAAGCCTGAAGAGCGACTTCTA
TCGTGCTCTGAGAGGGTATGACAGACAGTGCACCTCTTGTCAACAATTGTGACCGGA
ACGGTGAGCGTGCGTGTAACGGTGATTGCTCTTGCGAGGGCCAGATTTGTAAATGC
GGTTATAGAGTCAGTCCTGGGAAGTCAGGATGCGCGTGTACTTGTAGAAATGCCAA
ATGAATCATTTAACTCGTTGAAAGATTTTTTAAAAATCCAGAGCTATATGTTTCGAGA
AAAACCGAAGAC (SEQ ID NO:158)

Translation:

MMSKMGAMFVLLLLFTLASSQQEGDVQARKTSLKSDFYRALRGYDRQCTLVNNCDRN
GERACNGDCSCEGQICKCGYRVSPGKSGCACTCRNAK (SEQ ID NO:159)

Toxin Sequence:

Xaa2-Cys-Thr-Leu-Val-Asn-Asn-Cys-Asp-Arg-Asn-Gly-Xaa1-Arg-Ala-Cys-Asn-Gly-Asp-Cys-Ser-Cys-Xaa1-Gly-Gln-Ile-Cys-Lys-Cys-Gly-Xaa5-Arg-Val-Ser-Xaa3-Gly-Lys-Ser-Gly-Cys-Ala-Cys-Thr-Cys-Arg-Asn-Ala-Lys-^ (SEQ ID NO:160)

Name: Pn1.3
Species: pennaceus
Cloned: Yes

DNA Sequence:

ATGCGCTGTCTCCAGTCTTCGTCATTCTTCTGCTGCTGACTGCATCTGCACCTAGCG
TTGATGCCAAAGTTCATCTGAAGACCAAAGGTGATGGGCCCCTGTCATCTTTCCGAG
ATAATGCAAAGAGTACCCTACAAAGACTTCAGGACAAAAGCACTTGCTGTGGCTTT
AAGATGTGTATTCCTTGTCGTTAACCAGCATGAAGGATCC (SEQ ID NO:161)

Translation:

MRCLPVFVILLLLTASAPSVDAKVHLKTKGDGPLSSFRDNAKSTLQRLQDKSTCCGFKM
CIPCR (SEQ ID NO:162)

Toxin Sequence:

Ser-Thr-Cys-Cys-Gly-Phe-Lys-Met-Cys-Ile-Xaa3-Cys-Arg-^ (SEQ ID NO:163)

Name: Pn9.1
Species: pennaceus
Cloned: Yes

5 **DNA Sequence:**

ATGTTGCTTCTGCTGTTTGCCTTGGGCAGCTTCGTTGTGGTCCAGTCAGGACAGATA
 ACAAGAGATGTGGACAATGGGCAGCTCGCGGACAACCGCCGTACCCTGCGATCGCA
 GTGGAAGCAAGTGAGTTTCTTCAAGTCACTTGATAAACGACTGACTTGTAACGATCC
 TTGCCAGATGCATTCCGATTGCGGCATATGTGAATGCGTGGAAAATAAATGCATATT
 10 TTTTCATGTAAACGGATTGAGTTTGCTTGTC AACACAATGTCGCACTGCAGCTCTTCT
 CTACCGGTGGGTACATCGACCAAACGACGCATCTTTTATTTCTTTGTCTGTTTCGTTT
 GTTCTCCTGTGTTTATAACGTACAGAGCCCTTTAACTACCCTTACTGCTCTTCACTTA
 ACCTGATAACCTGAAGGTCCGGTGCAGCTGGCGTAGCCTTCACAGTTTCG (SEQ ID
 NO:164)

5 **Translation:**

MLLLLFALGSFVVVQSGQITRDVDNGQLADNRRTLRSQWKQVSFFKSLDKRLTCNDPC
 QMHSDCGICECVENKCIFFM (SEQ ID NO:165)

20 **Toxin Sequence:**

Leu-Thr-Cys-Asn-Asp-Xaa3-Cys-Gln-Met-His-Ser-Asp-Cys-Gly-Ile-Cys-Xaa1-Cys-Val-Xaa1-
 Asn-Lys-Cys-Ile-Phe-Phe-Met-^ (SEQ ID NO:166)

25 **Name:** Pu6.1
Species: pulicarius
Cloned: Yes

DNA Sequence:

30 ATGAAACTGACGTGTGTGGTGATCGTCGCCGTGCTGTTCTTGACGGCCTGTCAACTC
 AGTACAGCTGATGACTCCAGAGATGAGCAGCAGGATCCTTTGGTGAGGTTCGCATCG
 TGAGGAGCAGAAAGCCGAGGACCCCAAGACGGCCGAGAGATGTTTCAGATTTTCGGA
 TCCGACTGTGTTCTGCTACTCATAACTGCTGCAGTGGTGAATGTTTTGGCTTCGAG
 GACTTCGGCTTATGCACGTAAAACTGGTCTGACGTCTGATATTCCCCCCTCTGTCCTT
 35 CATCCTCTTTTGCCTGATTCATCCATACTATATGTGCTCCTGAACCGCTGTGTACCT
 TTACCTTGGTGGCTTCAGAGGACGTTATATCAAAATAAAACCGCGTTGCAATGACA
 AAAAAAAAAAAAAAAAAA (SEQ ID NO:167)

Translation:

40 MKLTCVVIVAVLFLTACQLSTADDSRDEQQDPLVRSHREEQKAEDPKTAERCSDFGSD
 CVPATHNCCSGECFGFEDFGLCT (SEQ ID NO:168)

Toxin Sequence:

45 Cys-Ser-Asp-Phe-Gly-Ser-Asp-Cys-Val-Xaa3-Ala-Thr-His-Asn-Cys-Cys-Ser-Gly-Xaa1-Cys-
 Phe-Gly-Phe-Xaa1-Asp-Phe-Gly-Leu-Cys-Thr-^ (SEQ ID NO:169)

Name: Bromosleeper-P1
Species: purpurascens
Cloned: Yes

5 **DNA Sequence:**

GACAGGATTGAACAAAATTCAGGATGTCAAGATTTGGAATCATGGTGCTAACCTTT
 CTACTTCTTGTGTCCATGGCAACCAGCCATCGTTATGCAAGAGGGAAGCAGGCGAC
 GCGAAGGAACGCAATCAACATCAGACGGAGAAGCACACCAAAAACTGAGGCGTGC
 GAAGAGGTCTGTGAGCTGGAAGAAAAGCACTGCTGCTGCATAAGAAGTGACGGAC
 10 CCAAATGTTCCCGTAAGTGCCTGTTGTCAATCTTCTGTTAGTTTCTGTACACTGTCTC
 ATTCATTATCTTATCAGTACAAGTGTAACGAGACATGTCAGAAAGTCGAAGGTTGT
 GCGTAATTTGATAAGTATTGTTTGCTGGGATGAACGGA (SEQ ID NO:170)

5 **Translation:**

MSRFGIMVLTFLLLVSMATSHRYARGKQATRRNAINIRRRSTPKTEACEEVCELEEKHC
 CCIRSDGPKCSRKCLLSIFC (SEQ ID NO:171)

20 **Toxin Sequence:**

Xaa3-Lys-Thr-Xaa1-Ala-Cys-Xaa1-Xaa1-Val-Cys-Xaa1-Leu-Xaa1-Xaa1-Lys-His-Cys-Cys-
 Cys-Ile-Arg-Ser-Asp-Gly-Xaa3-Lys-Cys-Ser-Arg-Lys-Cys-Leu-Leu-Ser-Ile-Phe-Cys-^ (SEQ ID
 NO:172)

25 **Name:** Bromosleeper-P2
Species: purpurascens
Cloned: Yes

30 **DNA Sequence:**

GACAGGATTGAACAAAATTCAGGATGTCAGGATTGGGAATCATGGTGCTAACCCCTT
 CTACTTCTTGTGTCCATGGCAACCAACCATCAGGATAGAGGAGAGAAGCAGGTGAC
 GCAAAGGGACGCAATCAACGTCAGACGGAGAAGATCAATCACCAGCAAGTCGTA
 TCTGAGGAGTGCAAAAAGTACTGTAAGAAACAGAACAAGAATTGCTGCAGCAGTAA
 ACATGAAGAACCCAGATGTGCCAAGATATGCTTCGGATAGTTTCTGTACACGGTCTC
 35 ATTCATTATTTTATCAGTACAAGTTAAACGAGACCTATCAGAAGTCGAAGGTTGTGC
 ATAATTTGATAAACATTGTTTGCTGGGATGAACGGA (SEQ ID NO:173)

40 **Translation:**

MSGLGIMVLTLTLLLVSMATNHQDRGEKQVTQRDAINVRRRRSITQQVVSEECKKYCKK
 QNKNCCSSKHIEPRCAKICFG (SEQ ID NO:174)

45 **Toxin Sequence:**

Val-Val-Ser-Xaa1-Xaa1-Cys-Lys-Lys-Xaa5-Cys-Lys-Lys-Gln-Asn-Lys-Asn-Cys-Cys-Ser-Ser-
 Lys-His-Xaa1-Xaa1-Xaa3-Arg-Cys-Ala-Lys-Ile-Cys-Phe-# (SEQ ID NO:175)

Name: P29
Species: purpurascens

Isolated: Yes

Toxin Sequence:

Asp-Cys-Cys-Gly-Val-Lys-Leu-Xaa1-Met-Cys-His-Xaa3-Cys-Leu-Cys-Asp-Asn-Ser-Cys-Lys-
5 Asn-Xaa5-Gly-Lys-# (SEQ ID NO:176)

Name: P4.1

Species: purpurascens

10 **Cloned:** Yes

DNA Sequence:

ATGTTACACCGTGTTTCTGTTGGTTGTCTTGGCAACCACTGTCGTTTCCTTCACTTCAG
ATCGTGCAATCGGATGACAGGAATACCAACGACAAAGCATCTCGCCTGCTCTCTCAC
5 GTTGTGAGGGGATGCTGTGGTAGCTATCCCAATGCTGCCTGTCATCCTTGCGGTTGT
AAAGATAGGCCATCGTATTGTGGTCAAGGACGCTGATGCTCCAGGACCCTCTGAAC
CACGACGT (SEQ ID NO:177)

Translation:

MFTVFLLVVLATTVVSFTSDRASDDRNTNDKASRLLSHVVRGCCGSSYPNAACHPCGCK
20 DRPSYCGQGR (SEQ ID NO:178)

Toxin Sequence:

Gly-Cys-Cys-Gly-Ser-Xaa5-Xaa3-Asn-Ala-Ala-Cys-His-Xaa3-Cys-Gly-Cys-Lys-Asp-Arg-
25 Xaa3-Ser-Xaa5-Cys-Gly-Gln-# (SEQ ID NO:179)

Name: P4.2

Species: purpurascens

30 **Cloned:** Yes

DNA Sequence:

ATGTTACACCGTGTTTCTGTTGGTTGTCTTGGCAACCACTGTCGTTTCCTTACCGTAG
ATCGTGCAACTGATGGCAGGAGTGCTGCAGCCATAGCGTTTGCCCTGATCGCTCCGA
35 CCGTCCGGGAAGGATGCTGTTCTAATCCTGCCTGTCATCCTTGCGGTTGTAAAGATA
GGCCATCGTATTGTGGTCAAGGACGCTGATGCTCCAGGACCCTCTGAACCACGACG
T (SEQ ID NO:180)

Translation:

MFTVFLLVVLATTVVSFTVDRATDGRSAAAIAFALIAPTVREGCCSNPACHPCGCKDRP
40 SYCGQGR (SEQ ID NO:181)

Toxin Sequence:

Xaa1-Gly-Cys-Cys-Ser-Asn-Xaa3-Ala-Cys-His-Xaa3-Cys-Gly-Cys-Lys-Asp-Xaa3-Ser-
45 Xaa5-Cys-Gly-Gln-# (SEQ ID NO:182)

Name: P8.1
Species: purpurascens
Cloned: Yes

5 **DNA Sequence:**

ATGATGTCGAAAATGGGAGCTATGTTTGTCTTTTGTCTCTTTTCACCCTGGCATCCA
GCCAGCAGGAAGGAGATGTCCAGGCAAGGAAAACACGCCTGACGAGGGACTTCTA
TCGTACTCTGCCAGTGTCTACTAGAGGATGCAGCGGCTCCCCTTGTTTTAAAAACAA
AACGTGTCTGGGATGAATGCATATGCGGCGGCTTATCCAATTGTTGGTGTGGCTACGG
10 CGGTAGTCGAGGATGCAAGTGTACATGTAGAGAGTGATTAATCGACTCTTTAACTC
GTTGAATTATTAAAAAATCCAGAGCAATATGTTTCGAGAAAAACCGAAGAC (SEQ ID
NO:183)

Translation:

MMSKMGAMFVLLLLFTLASSQQEGDVQARKTRLTRDFYRTLVPVSTRGCSGSPCFKNKT
CRDECICGGLSNCWCGYGGSRGCKCTCRE (SEQ ID NO:184)

Toxin Sequence:

Gly-Cys-Ser-Gly-Ser-Xaa3-Cys-Phe-Lys-Asn-Lys-Thr-Cys-Arg-Asp-Xaa1-Cys-Ile-Cys-Gly-
Gly-Leu-Ser-Asn-Cys-Xaa4-Cys-Gly-Xaa5-Gly-Gly-Ser-Arg-Gly-Cys-Lys-Cys-Thr-Cys-Arg-
Xaa1-^ (SEQ ID NO:185)

Name: U021 homolog
Species: purpurascens
Cloned: Yes

DNA Sequence:

CGACCTCAAGAGGGATCGATAGCAGTTCATGATGTCTAAACTGGGAGCCTTGTTGA
30 CCATCTGTCTGCTTCTGTTTCCCATTACTGCTCTTCTGATGGATGGAGATCAACCTGC
AGACCGACCTGCAGAACGTATGGATTACGACATTTTCATCTGAGGTGCATCGTTTGCT
TGAAAGGAGACACCCGCCCTGTTGCATGTACGGCAGATGCCGTCGATATCCCGGAT
GCTCTAGTGCCTCTTGTTGCCAGGGAGGATAACGTGTTGATGACCAACTTTGTTACA
CGGCTACGTCAAGTGTCTACTGAATAAGTAAAACGATTGCAGT (SEQ ID NO:186)

Translation:

MMSKLGALLTICLLFPITALLMDGDQPADRP AERMDYDISSEVHRLLERRHPPCCMYG
RCRRYPGCSSASCCQGG (SEQ ID NO:187)

40 **Toxin Sequence:**

His-Xaa3-Xaa3-Cys-Cys-Met-Xaa5-Gly-Arg-Cys-Arg-Arg-Xaa5-Xaa3-Gly-Cys-Ser-Ser-Ala-
Ser-Cys-Cys-Gln-Gly-# (SEQ ID NO:188)

45 **Name:** ψ -PIIIF
Species: purpurascens

Isolated: Yes

Toxin Sequence:

5 Gly-Xaa3-Xaa3-Cys-Cys-Leu-Xaa5-Gly-Ser-Cys-Arg-Xaa3-Phe-Xaa3-Gly-Cys-Xaa5-Asn-Ala-Leu-Cys-Cys-Arg-Lys-# (SEQ ID NO:189)

Name: Qc6.4

10 **Species:** quercinus

Cloned: Yes

DNA Sequence:

GGATCCATGAAACTGACGTGCGTGGTGATCATCGCCGTGCTGTTTCTGACAGCCAGT
5 CAGCTCGTTACAGCTGATTACACCAGAGATAAATGGCAATACCCTGCAGCGAGTTT
GAGAGGCGGAATGTGGAATTTGAGAGATACCAGGGCGTGCTCGCAAGTAGGTGAA
GCTTGTTTTCTCAGAAACCTTGCTGCCCTGGATTCTTTGCAATCACATCGGAGGC
ATGTGCCACCACTAGTAACAGTCTGGCATCTGATATTTCCCCTCTGCGCTCCACCCT
CTTTTGGCTGATTCATCCTTACCTGTGTGTGGTCATGAACCACTCAGTAGCTACACCT
20 CTGGTGGCTTCAGAGGACGTATATCAAAATAAAACCACATTGCAAAAAAAAAAAAAA
AAAA (SEQ ID NO:190)

Translation:

MKLTCVVIIAVLFLTASQLVTADYTRDKWQYPAASLRGGMWNLRDTRACSQVGEACF
25 PQKPCCPGFLCNHIGGMCHH (SEQ ID NO:191)

Toxin Sequence:

Ala-Cys-Ser-Gln-Val-Gly-Xaa1-Ala-Cys-Phe-Xaa3-Gln-Lys-Xaa3-Cys-Cys-Xaa3-Gly-Phe-
30 Leu-Cys-Asn-His-Ile-Gly-Gly-Met-Cys-His-His-^ (SEQ ID NO:192)

Name: QcII

Species: quercinus

Isolated: Yes

Toxin Sequence:

Asp-Cys-Gln-Xaa3-Cys-Gly-His-Asn-Val-Cys-Cys-^ (SEQ ID NO:193)

40 **Name:** EST171

Species: radiatus

Cloned: Yes

DNA Sequence:

45 CATGAAGTGTCTCGTACTGGCTTTGGTTACCATCGGTCTTCTGGCTGCAACAACCGC
AGCCCCTCTGGACACCACCACGGTCCTCCTCAGCACAACCTACACGCGATGTCAAGG
GCTGTGTGTACGAGGGCATAGAGTACAGTGTCTGGAGAGACCTACCAGGCAGACTGC

AACACGTGTCGCTGTGATGGCTTTGACCTGGCTACATGCACCGTCGCGGGCTGCACA
GGCTTTGGACCCGAGTGATTGGTACTATTCCACACCTAGCAATGTTTCACTGGAAC
CGGAACCTTGATACTACCTTCTAAATATAATCAATTTGTTTCAAAAGGCCCAA (SEQ
ID NO:194)

Translation:

MNCLVLALVTIGLLAATTAAPLDTTTLVLLSTTTRDVKGCVYEGIEYSVGETYQADCNTC
RCDGFDLATCTVAGCTGFGPE (SEQ ID NO:195)

Toxin Sequence:

Gly-Cys-Val-Xaa5-Xaa1-Gly-Ile-Xaa1-Xaa5-Ser-Val-Gly-Xaa1-Thr-Xaa5-Gln-Ala-Asp-Cys-
Asn-Thr-Cys-Arg-Cys-Asp-Gly-Phe-Asp-Leu-Ala-Thr-Cys-Thr-Val-Ala-Gly-Cys-Thr-Gly-Phe-
Gly-Xaa3-Xaa1-^ (SEQ ID NO:196)

Name: EST202

Species: radiatus

Cloned: Yes

DNA Sequence:

GTGAGAGTCCAACAGCCCCAACCTTTCAACTCACTATGTGGCAGTTGCAGTTTTCAA
CGTCTGGACAGGATTCAACAAAATTCAGGATGTCAGGATTGGGAATCATGGTGCTA
ACCCTTCTACTTCTTGTGTCCATGGCAACCAGTCGTCAGGATAGAGGAGTGGGACAG
CTGATGCCACGCGTCTCGTTCAAAGCCTGCAAATCAAATTATGATTGCCCCCAGCGT
TTCAAATGCTGCAGTTACACCTGGAATGGATCCAGTGGATACTGTAAACGTGTTTGC
TATCTTTATCGTTAGTGTAATACACAAAGTGACTCTGTTCATTCTCTCCATCATCTC
TTTAGAAACAACACGGTGTGCGAGATCGTTTCTTTGTGATGAAGAGTAGTATCACGGG
CAGAGTTCACTAGAGATCTCAAATGAAAAACAAGATTATTTAGTAAGTTGGGGAAA
ATCTGGATCTCGAAAAGATTCCTTGAAAACCTCCGTATTTAACACGCTTGAGAGATGA
TAATAAAGAATTCTGAAAGACaAA (SEQ ID NO:197)

Translation:

MSGLGIMVLTLILLVSMATSRQDRGVGQLMPRVSEFKACKSNYDCPQRFKCCSYTWNG
SSGYCKRVCYLYR (SEQ ID NO:198)

Toxin Sequence:

Ala-Cys-Lys-Ser-Asn-Xaa5-Asp-Cys-Xaa3-Gln-Arg-Phe-Lys-Cys-Cys-Ser-Xaa5-Thr-Xaa4-
Asn-Gly-Ser-Ser-Gly-Xaa5-Cys-Lys-Arg-Val-Cys-Xaa5-Leu-Xaa5-Arg-^ (SEQ ID NO:199)

Name: R8.1

Species: radiatus

Cloned: Yes

DNA Sequence:

ATGATGTCGAAAATGGGAGCTATGTTTGTCTTTTGCTTCTTTTCACCCTGGCATCCA
GCCAGCAGGAAGGAGATGTCCAGGCAAGGAAAACACACCCGAAGAGAGAGTTCCA

ACGTATTCTGCTAAGGTCTGGCAGAAAGTGCAATTTTCGACAAATGTAAAGGTACCG
 GAGTCTACAATTGTGGGGAATCCTGCTCATGCGAAGGTTTGCACAGTTGTCGCTGCA
 CTTATAACATCGGTTCTATGAAGTCTGGATGCGCGTGTATTTGTACATACTATTAAT
 GATTAATTGACTCGTTTAACTCGTTGAACGATTAAAAAATCCAGAGCAATATGTTTC
 5 GAGAAAAACCGAAGAC (SEQ ID NO:200)

Translation:

MMSKMGAMFVLLLLFTLASSQQEGDVQARKTHPKREFQRILLRSGRKCNFDKCKGTG
 VYNCGESCSCEGLHSCRCTYNIGSMKSGCACICTYY (SEQ ID NO:201)

Toxin Sequence:

Lys-Cys-Asn-Phe-Asp-Lys-Cys-Lys-Gly-Thr-Gly-Val-Xaa5-Asn-Cys-Gly-Xaa1-Ser-Cys-Ser-
 Cys-Xaa1-Gly-Leu-His-Ser-Cys-Arg-Cys-Thr-Xaa5-Asn-Ile-Gly-Ser-Met-Lys-Ser-Gly-Cys-
 Ala-Cys-Ile-Cys-Thr-Xaa5-Xaa5-^ (SEQ ID NO:202)

Name: R8.2

Species: radiatus

Cloned: Yes

DNA Sequence:

ATGATGTCGAAAATGGGAGCTATGTTTGTCTTTTGTCTTTTTCACCCTGGCATCCA
 GGCAGCAGGAAGGAGATGTCCAGGCAAGGAAAAACACGCCTGACGAGCGACTTCTA
 TAGTGTTCTGCAAAGGTATGGACTAGGATGCGCTGGCACTTGTGGTTCAAGCAGCA
 ATTGTGTTAGAGATTATTGTGACTGCCCAAAACCCAATTGTTACTGCACTGGCAAAG
 GCTTTCGTCAACCAGGATGCGGGTGTTCATGTTTGGGGTGATTAATTGGCTCTTTTA
 ACTCGTTGAACGATTAAAAAATCCAGAGCAATATGTTTCGAGAAAAACCGAAGAC
 (SEQ ID NO:203)

Translation:

MMSKMGAMFVLLLLFTLASRQQEGDVQARKTRLTSDFYSLQRYGLGCAGTCGSSSN
 CVRDYCDCPKPNCYCTGKGFRQPGCGCSCLG (SEQ ID NO:204)

Toxin Sequence:

Xaa5-Gly-Leu-Gly-Cys-Ala-Gly-Thr-Cys-Gly-Ser-Ser-Ser-Asn-Cys-Val-Arg-Asp-Xaa5-Cys-
 Asp-Cys-Xaa3-Lys-Xaa3-Asn-Cys-Xaa5-Cys-Thr-Gly-Lys-Gly-Phe-Arg-Gln-Xaa3-Gly-Cys-
 Gly-Cys-Ser-Cys-Leu-# (SEQ ID NO:205)

Name: Bromosleeper-Sn

Species: sponsalis

Cloned: Yes

DNA Sequence:

GACAGGATTGAACAAAATTCAGGATGTCAGGATTGGGAATCATGGTGCTGACCCTT
 TTGCTTCTTGTGTCCATGGCAACCAGCCATAAGGATGGAGGAGAGAAGCAGGCGAT
 GCAAAGGGACGCAATCAACGTCAGACTGAGAAGATCACTCACTCGGAGAGCAGTA

ACTGAGGCGTGACGGAGGACTGTAAGACTCAGGACAAGAAGTGCTGCGGGCGAAA
TGAATGGACAACACACATGTGCCAAGATATGCCTCGGATAGTCTCTGTACGCTGTCT
CATTTCATTATCTCATCAGTACAAGTGTAACGAGACAGGTCAGAAAGTCGAAGGTT
GTTTCGAAATTTGATAAGCATTGTTTACTGGGACGAACGGA (SEQ ID NO:206)

Translation:

MSGLGIMVLTLTLLLVSMATSHKDGGEKQAMQRDAINVRLRRSLTRRAVTEACTEDCKT
QDKKCCGEMNGQHTCAKICLG (SEQ ID NO:207)

Toxin Sequence:

Ala-Val-Thr-Xaa1-Ala-Cys-Thr-Xaa1-Asp-Cys-Lys-Thr-Gln-Asp-Lys-Lys-Cys-Cys-Gly-Xaa1-
Met-Asn-Gly-Gln-His-Thr-Cys-Ala-Lys-Ile-Cys-Leu-# (SEQ ID NO:208)

Name: Contryphan-Sm-dW4, V7
Species: stercusmuscarum
Isolated: Yes

Toxin Sequence:

Gly-Cys-Xaa3-Xaa4-Gln-Xaa3-Val-Cys-# (SEQ ID NO:209)

Name: Conopressin-S
Species: striatus
Isolated: Yes

Toxin Sequence:

Cys-Ile-Ile-Arg-Asn-Cys-Xaa3-Arg-Gly-# (SEQ ID NO:210)

Name: S6.4
Species: striatus
Cloned: Yes

DNA Sequence:

AGGTCGACTCGCTGCTTGCCTGACGGAACGTCTTGCCTTTTTAGTAGGATCAGATGC
TGCGGTACTTGAGTTCAATCTTAAAGTCATGTGTGAGCTGATCCAGCGGTTGATCT
TCCTCCCTCTGTGCTCCATCCTTTTCTGCCTGAGTTCTCCTTACCTGAGAGTGGTCAT
GAACCACTCATCACCTACTCTTCTGGAGGCTTCAGAGGAGCTACAGTGAAATAAAA
GCCGCATTGC (SEQ ID NO:211)

Translation:

STRCLPDGTSCLF SRIRCCGTCSSILKSCVS (SEQ ID NO:212)

Toxin Sequence:

Cys-Leu-Xaa3-Asp-Gly-Thr-Ser-Cys-Leu-Phe-Ser-Arg-Ile-Arg-Cys-Cys-Gly-Thr-Cys-Ser-Ser-Ile-Leu-Lys-Ser-Cys-Val-Ser-^ (SEQ ID NO:213)

5 **Name:** U010 homolog
Species: striatus
Cloned: Yes

DNA Sequence:

10 CGGCTTCTAATACGACTCACTATAGGGCAAGCAGTGGTAACAACGCAGAGTACGCG
 GGGGGACGGCAGACCAGCTGGGGACCAGACAGACGTCAAACAGCATCGCAGTCAG
 GTGTGGAGATCCCAAGACACCCAGAAGAAGGAGACAGAAGAGTTATCGTTCGTAAC
 ACAATGGCCATGAACATGTCGATGACACTCTGCATGTTTGTAATGGTCGTCGTGGCA
 GCCACTGTCAATTGATTCCACTCAGTTACAAGAACCAGATCTCAGTCGCATGCGACGC
 15 AGCGGGCCTGCTGACTGTTGCAGGATGAAAGAGTGTTGCACCGACAGAGTGAACGA
 GTgTCTACAGCGCTATTCTGGCCGGGAAGATAAAATTCGTTTCGTTTTGTTATCAGGA
 GGCCACAGTCACATGTGGATCTTTTAACGAAATCGTGGGCTGTTGCTATGGATATCA
 AATGTGCATGATACGAGTTGTGAAACCGAACAGTCTAAGTGGGGCCCATGAGGCGT
 GCAAAACCGTTTCTTGTGGTAACCCCTTGCGCTTGAGGTGTCCTCGCGCCACGTCACC
 20 TGTGTACAGCGCCGTCACCAGAGCCCTGATCTTTATGCCCTTATCTGTCTTTTGTCTC
 TTTCACTCTCTGAAGTCTTGAGGTTTGTTCATTCTTGTCAATCATCTCACGCGCATC
 CAAGTAAATAAAGGTGACGTGACAAAC (SEQ ID NO:214)

Translation:

25 MAMNMSMTLCMFVMVVVAATVIDSTQLQEPDLSRMRRSGPADCCRMKECCTDRVNE
 CLQRYSGREDKFVSFCYQEATVTCGSFNEIVGCCYGYQMCMIRVVKPNLSGAHEACK
 TVSCGNPCA (SEQ ID NO:215)

Toxin Sequence:

30 Ser-Gly-Xaa3-Ala-Asp-Cys-Cys-Arg-Met-Lys-Xaa1-Cys-Cys-Thr-Asp-Arg-Val-Asn-Xaa1-
 Cys-Leu-Gln-Arg-Xaa5-Ser-Gly-Arg-Xaa1-Asp-Lys-Phe-Val-Ser-Phe-Cys-Xaa5-Gln-Xaa1-
 Ala-Thr-Val-Thr-Cys-Gly-Ser-Phe-Asn-Xaa1-Ile-Val-Gly-Cys-Cys-Xaa5-Gly-Xaa5-Gln-Met-
 Cys-Met-Ile-Arg-Val-Val-Lys-Xaa3-Asn-Ser-Leu-Ser-Gly-Ala-His-Xaa1-Ala-Cys-Lys-Thr-Val-
 Ser-Cys-Gly-Asn-Xaa3-Cys-Ala-^ (SEQ ID NO:216)

35

Name: WG002
Species: striatus
Isolated: Yes

40

Toxin Sequence:

Xaa4-Ser-Xaa4-Arg-Met-Gly-Asn-Gly-Asp-Arg-Arg-Ser-Asp-Gln-^ (SEQ ID NO:217)

45 **Name:** Sx8.1
Species: striolatus
Cloned: Yes

DNA Sequence:

ATGATGTCGAAAATGGGAGCTATGTTTGTCTTTTGCTTCTTTTGACCCTGGCATCCA
 GCCAGCAGGAGGGAGATGTCCAGGCAAGGAAAACAAGCCTGAAGAGCGACTTCTA
 5 TCGTGCTCTGAGACCGTATGACAGACAGTGCACCTTTTGTCAACAATTGTCAACAGAA
 CGGTGCGTGTAACGGTGATTGCTCTTGCGGGGACCAGATTTGTAAATGCGGTTATAG
 AATCAGTCCTGGGAGGTCAGGATGCGCGTGTACTTGTAGAAATGCCAAATGAATCA
 CTTAACTCGTTGAAAGATTTTAAAAATCCAGAGCTATATGTTCGAGAAAAACCGA
 AGAC (SEQ ID NO:218)

Translation:

MMSKMGAMFVLLLLTLASSQQEGDVQARKTSLKSDFYRALRPYDRQCTFVNNCQQN
 GACNGDCSCGDQICKCGYRISPGRSGCACTCRNAK (SEQ ID NO:219)

Toxin Sequence:

Xaa2-Cys-Thr-Phe-Val-Asn-Asn-Cys-Gln-Gln-Asn-Gly-Ala-Cys-Asn-Gly-Asp-Cys-Ser-Cys-
 Gly-Asp-Gln-Ile-Cys-Lys-Cys-Gly-Xaa5-Arg-Ile-Ser-Xaa3-Gly-Arg-Ser-Gly-Cys-Ala-Cys-Thr-
 Cys-Arg-Asn-Ala-Lys-^ (SEQ ID NO:220)

Name: Ts6.3

Species: tessulatus

Cloned: Yes

DNA Sequence:

GGATCCATGAAACTGACGTGTGTGGTGATCATCGCCGTGCTGTTCTGACGGCCTGT
 CAATTCATTATAGCTGATTTCTCCAGAGATAAGCGGGTACATCGTGACAGAGAGGTTG
 AGAGACATAATGCAGAATTCAGAGGTACCAGGTCGTGCGCGGAATTTGGTGAAGT
 TTGTAGTTCTACCGCTTGCTGCCCTGATTTGGATTGCGTTGAGGCCTATTCACCCATC
 30 TGTCTCTGGGAATAGTCTGGCATCTGATATTTCCCGTCTGTGCTCTACCTACTTCTGC
 CGGATTCATCCATACCTATGTGTGGCCATGAACCACTCAGTACCTACACCTCTGGTG
 GCTTCCTAGGGACGTATATCAAAATAAAACCACATTGCAAAAAAAAAAAAAAAAAAAAA
 (SEQ ID NO:221)

Translation:

MKLTCVVIIAVLFLTACQFIADFSRDKRVHRAERLRDIMQNFRGTRSCAEFGEVCSSTA
 CCPDLDCVEAYSPICLWE (SEQ ID NO:222)

Toxin Sequence:

Ser-Cys-Ala-Xaa1-Phe-Gly-Xaa1-Val-Cys-Ser-Ser-Thr-Ala-Cys-Cys-Xaa3-Asp-Leu-Asp-Cys-
 Val-Xaa1-Ala-Xaa5-Ser-Xaa3-Ile-Cys-Leu-Xaa4-Xaa1-^ (SEQ ID NO:223)

Name: 4/43 SNX

Species: textile

Isolated: Yes

Cloned: Yes

DNA Sequence:

CGATTGCAGGGGTTaCGATGCGCCGTGTAGCTCTGGCGCGCCATGTTGTGATTGGTG
 GACATGTTTCAGCACGAACCAACCGCTGTTTTTAGGCTGACCACAAGCCATCCGACAT
 5 CACCACTCTCCTCTTCAGAGGCTTCAAGGCTTTTTGTTCTCCTTTTGAAGAATCTTTA
 CGAGTGAACAAACAAGTAGAATAGCACGTTTTTCCCCCTTTGAAAAATCAATAATG
 GAGGTAAACAAAACACTGTCTTCTTCAATAAAGATTTTATCATAAT (SEQ ID NO:224)

Translation:

10 IQGGGDERQKAKINFLSRSDRDCRGYDAPCSSGAPCCDWWTCSARTNRCF (SEQ ID
 NO:225)

Toxin Sequence:

Asp-Cys-Arg-Gly-Xaa5-Asp-Ala-Xaa3-Cys-Ser-Ser-Gly-Ala-Xaa3-Cys-Cys-Asp-Xaa4-Xaa4-
 5 Thr-Cys-Ser-Ala-Arg-Thr-Asn-Arg-Cys-Phe-^ (SEQ ID NO:226)

Name: convulsion

Species: textile

Isolated: Yes

Toxin Sequence:

Asn-Cys-Xaa3-Xaa5-Cys-Val-Val-Xaa5-Cys-Cys-Xaa3-Xaa3-Ala-Xaa5-Cys-Xaa1-Ala-Ser-
 Gly-Cys-Arg-Xaa3-Xaa3-# (SEQ ID NO:227)

Name: Tx1.6

Species: textile

Cloned: Yes

DNA Sequence:

ATGCACTGTCTCCCAATCTTCGTCATTCTTCTGCTGCTGACTGCATCTGGACCTAGCG
 TTGATGCCCAACTGAAGACCAAAGATGATGTGCCCCTGTCATCTTTCCGAGATCATG
 CAAAGAGTACCCTACGAAGACTTCAGGACAAACAGACTTGCTGTGGCTATAGGATG
 35 TGTGTTCCCTTGTGGTTAACCAGCATGAAGGATCC (SEQ ID NO:228)

Translation:

MHCLPIFVILLLLTASGPSVDAQLKTKDDVPLSSFRDHAKSTLRRLQDKQTCCGYRMCV
 PCG (SEQ ID NO:229)

Toxin Sequence:

Xaa2-Thr-Cys-Cys-Gly-Xaa5-Arg-Met-Cys-Val-Xaa3-Cys-# (SEQ ID NO:230)

Name: Tx6.14

Species: textile

Cloned: Yes

DNA Sequence:

GTTATGGAGCGATTGCTATAGTTGGTTAGGATCATGTATTGCGCCCTCGCAGTGTTG
 TTCTGAGGTTTGTGATTATTACTGCCGCCTATGGCGATGAACTCGGACCACAAGCCA
 T (SEQ ID NO:231)

Translation:

LWSDCYSWLGSCIAPSQCCSEVCDYYCRLWR (SEQ ID NO:232)

Toxin Sequence:

Asp-Cys-Xaa5-Ser-Xaa4-Leu-Gly-Ser-Cys-Ile-Ala-Xaa3-Ser-Gln-Cys-Cys-Ser-Xaa1-Val-Cys-
 Asp-Xaa5-Xaa5-Cys-Arg-Leu-Xaa4-Arg-^ (SEQ ID NO:233)

Name: Tx6.3
Species: textile
Cloned: Yes

DNA Sequence:

AGCTGACGAATGAAAAATTCCGAGAATGTCAAGCTCAGCAAGAGAAAAATGTGTGGA
 ACAATGGAAATACTGCACCCGAGAGTCCTTATGTTGCGCGGGTTTGTGTTTGTTTAG
 TTTCTGCATTCTATAACGCTAATCCAGAGTCGTATATTCCGTCTAAGCTCCACCTGGC
 ACTGTCTGGTATGTTTCTGCCAGTGACTGGTCTCATACCGCTTAGACTCTGGTCCGTC
 TTCTCTGCAACCACAGGAGAACGTGCATTATTACAATAAACGCATACTGC (SEQ ID
 NO:234)

Translation:

RMKNSENVKLSKRKCVEQWKYCTRESLCCAGLCLFSFCIL (SEQ ID NO:235)

Toxin Sequence:

Lys-Cys-Val-Xaa1-Gln-Xaa4-Lys-Xaa5-Cys-Thr-Arg-Xaa1-Ser-Leu-Cys-Cys-Ala-Gly-Leu-
 Cys-Leu-Phe-Ser-Phe-Cys-Ile-Leu-^ (SEQ ID NO:236)

Name: Tx6.7
Species: textile
Cloned: Yes

DNA Sequence:

CAGAGCCGCTCTGGTGTGCAGACCTGTCTCCAGCCCTCCGTCTCCCTGATCGGTGGT
 TCTGCCTGCATAGCTGTCTTCTCCACGAAGCTTTCCACAGGTATAAATAACGCTTCA
 GTCTCCCGTCCTGTATTGGGCCGCCGTTACAAGCCAGACCGATAACAGCCAGGTCCA
 GTCTACTTTGCGAGTGAGTTAAAAGCTCCAGCATTCTACCAGCATCACCAGAATGAA
 GGTGAGCAGCGTGCTGATCGTGGCTACGCTGACACTGACCGCAGGCCAGCTGGTTA
 GTGCTTCTTCCCATTACTCAAAAGATGTCCAGATTCTTCCTTCTGTGAGATCAGCTGA
 CGAAGTGGAATAATTCCGAGAATGTCAGGCTCAGCAAGAGAAGATGTGTGGAACAAT

GGGAAGTCTGCGGCATAATCTTGTTCTCCTCATCATGTTGCGGGCAGTTGTGTTTGT
TGGTTTCTGCGTTCTATAACGCTAATCCAGAGTCGTATATTCCGTCTAAGCTCCA
(SEQ ID NO:237)

5 **Translation:**

MKVSSVLIVATLTLTAGQLVSASSHYSKDVQILPSVRSADENVRLSKRRCVEQW
EVCGIILFSSSCCGQLCLFGFCVL (SEQ ID NO:238)

Toxin Sequence:

10 Cys-Val-Xaa1-Gln-Xaa4-Xaa1-Val-Cys-Gly-Ile-Ile-Leu-Phe-Ser-Ser-Ser-Cys-Cys-Gly-Gln-
Leu-Cys-Leu-Phe-Gly-Phe-Cys-Val-Leu-^ (SEQ ID NO:239)

Name: TxVIIA

Species: textile

Isolated: Yes

Toxin Sequence:

Cys-Gly-Gly-Xaa5-Ser-Thr-Xaa5-Cys-Xaa1-Val-Asp-Ser-Xaa1-Cys-Cys-Ser-Asp-Asn-Cys-
Val-Arg-Ser-Xaa5-Cys-Thr-Leu-Phe-# (SEQ ID NO:240)

Name: U030

Species: textile

Isolated: Yes

Toxin Sequence:

Gly-Cys-Asn-Asn-Ser-Cys-Gln-Xaa1-His-Ser-Asp-Cys-Xaa1-Ser-His-Cys-Ile-Cys-Thr-Ser-
Arg-Gly-Cys-Gly-Ala-Val-Asn-# (SEQ ID NO:241)

Name: Bromosleeper-T1

Species: tulipa

Cloned: Yes

DNA Sequence:

35 CAGGATTGAACAAAATTCAGGATGTCAGGATTGGGAATCATGGTGCTAACCCTTCT
ACTTCTTGTGTCCATGGCAACCAGTCATCGTTATGCAAGAGAAAAGCAGGCGACGC
GAAGGGACGCAGTCAACGTCAGACGGAGAAGCAGACCAAAAACAAAGGAGTGCGA
AAGGTACTGTGAGCTGGAGGAAAAGCACTGCTGCTGCATAAGAAGTAACGGACCCA
AATGTTCCAGAATATGCATATTCAAATTTTGGTGTTAGTTTTCTGTACACTGTCCATT
CATTATCTTATCAGTACAAGTGTAACGAGACATGTCAGAAAGTCGAAGGTTGTGC
40 GTAATTTGATAAGCATTGTTTACTGGGACGAACGGA (SEQ ID NO:242)

Translation:

MSGLGIMVLTLTLLLVSMATSHRYAREKQATRRDAVNVRRRSRPKTKECERYCELEEKH
CCCIRSNGPKCSRICIFKFWC (SEQ ID NO:243)

Toxin Sequence:

Xaa3-Lys-Thr-Lys-Xaa1-Cys-Xaa1-Arg-Xaa5-Cys-Xaa1-Leu-Xaa1-Xaa1-Lys-His-Cys-Cys-Cys-Ile-Arg-Ser-Asn-Gly-Xaa3-Lys-Cys-Ser-Arg-Ile-Cys-Ile-Phe-Lys-Phe-Xaa4-Cys-^ (SEQ ID NO:244)

5 **Name:** Bromosleeper-T2
Species: tulipa
Cloned: Yes

DNA Sequence:

10 CAGGATTGAACAAAATTCAGGATGTCAGGATTGGGAATCATGGTGCTAACCCCTTCT
 CCTTCTTGTGCTAATGACAACCAGTCATCAGGATGCAGGAGAGAAGCAGGCGATGC
 AAAGGGACGCAAAGAACTTCAGTCGGAGAAGATTAGTCATTCGGAGACCAAAAAC
 AAGGGAGTGCGAAATGCAGTGTGAGCAGGAGGAGAAACACTGCTGCCGCGTAAGA
 GATGGTACGGGCCAATGTGCCCCCTAAGTGCTTGGGAATTAAGTGGTAGTTTCTGTAC
 5 ACTGTCTCATTATTATCTTATCAGTACACGTGTAACGAGACATGTCAGAAAGTCGA
 AGGTAGTGCCTAATTTGATAAGCATTGTTTACTGGGACGAACGGA (SEQ ID NO:245)

Translation:

20 MSGLGIMVLTLTLLVLMTTSHQDAGEKQAMQRDAKNFSRRRLVIRRPKTRECEMQCEQ
 EEKHCCRVRDGTGQCAPKCLGINW (SEQ ID NO:246)

Toxin Sequence:

25 Xaa3-Lys-Thr-Arg-Xaa1-Cys-Xaa1-Met-Gln-Cys-Xaa1-Gln-Xaa1-Xaa1-Lys-His-Cys-Cys-Arg-
 Val-Arg-Asp-Gly-Thr-Gly-Gln-Cys-Ala-Xaa3-Lys-Cys-Leu-Gly-Ile-Asn-Xaa4-^ (SEQ ID
 NO:247)

30 **Name:** T8.1
Species: tulipa
Cloned: Yes

DNA Sequence:

35 ATGATGTCGAAAATGGGAGCTATGTTTGTCTTTTGCTTCTTTTCACCCTGGCATCCA
 GCCAGCAGGAAGGAGATGTCCAGGCAAGGAAAACACGCCTGAAGAGCGACTTCTA
 TCGTGCTCTGCCAAGGTTTGGCCCAATATGCACTTGTTTTAAAGCCAGAACTGTCTG
 GGGTTCTTGTGAATGCATGTACCTCCCGGTTGTTACTGCAGTAACAATGGCATTCTG
 TGAACGAGGATGCTCGTGTACATGTCCAGGGACTGGTTGAATGATTTGAAAAATTC
 AGAGCAATATGTTGCAGAAAAACCGAAGACCGAGACTTCTCACAATAAATCCATAA
 AGACATTAAAAA (SEQ ID NO:248)

Translation:

40 MMSKMGAMFVLLLLFTLASSQQEGDVQARKTRLKSDFYRALPRFGPICTCFKSQNCRG
 SCECMSPPGCYCSNNGIRERGCSTCPGTG (SEQ ID NO:249)

Toxin Sequence:

45 Phe-Gly-Xaa3-Ile-Cys-Thr-Cys-Phe-Lys-Ser-Gln-Asn-Cys-Arg-Gly-Ser-Cys-Xaa1-Cys-Met-
 Ser-Xaa3-Xaa3-Gly-Cys-Xaa5-Cys-Ser-Asn-Asn-Gly-Ile-Arg-Xaa1-Arg-Gly-Cys-Ser-Cys-Thr-
 Cys-Xaa3-Gly-Thr-# (SEQ ID NO:250)

Name: T8.2
Species: tulipa
Cloned: Yes

DNA Sequence:

ATGATGTCGAAAATGGGAGCTATGTTTGTCTTTTGCTTCTTTTCACCCTGGCATCCA
GCCAGCAGGAAGGAGATGTCCAGGCAAGGAAAACACGCCTGAAGAGCGACTTCTA
TCGTACTCTGGCAATATCTGACAGAGGATGCACTGGCAACTGTGATTGGACGTGTA
GCGGTGATTGCAGCTGCCAGGGCACATCTGACTCGTGTCACTGCATTCCACCAAAT
CAATAGGCAACAGATGCCGGTGTCAAGTGTAAAAGAAAAATCGAAATTGACTGATTC
TTTAACTCGTTGAACGATTTAAAAATCAGACCAATATGTAGGCAGAAAACCGAAG
ACTCTGAGACTCTCGTAATAATCGTAAGCAAAAAAAAAAAAAAAAAAAAA (SEQ ID NO:251)

Translation:

MMSKMGAMFVLLLLFTLASSQQEGDVQARKTRLKSDFYRTLAIISDRGCTGNCDWTCS
GDCSCQGTSDSCHCIPPKSIGNRCRCQCKRKIEID (SEQ ID NO:252)

Toxin Sequence:

Gly-Cys-Thr-Gly-Asn-Cys-Asp-Xaa4-Thr-Cys-Ser-Gly-Asp-Cys-Ser-Cys-Gln-Gly-Thr-Ser-
Asp-Ser-Cys-His-Cys-Ile-Xaa3-Xaa3-Lys-Ser-Ile-Gly-Asn-Arg-Cys-Arg-Cys-Gln-Cys-Lys-
Arg-Lys-Ile-Xaa1-Ile-Asp-^ (SEQ ID NO:253)

Name: Vr6.1
Species: virgo
Cloned: Yes

DNA Sequence:

GGATCCATGAAACTGACGTGTGTGGTGATCATCACTGTGCTGTTTCCTGACGGCCAGT
CAGCTCATTACAGCTGATTACTCCAGAGATCAGCGGCAGTACCGTGCAGTGAGGTT
GGGAGATGAAATGCGGAATTTCAAAGGTGCCAGGGACTGCGGGGGACAAGGTGAA
GGTTGTTATACTCAACCTTGCTGCCCTGGTCTGCGGTGCCGTGGCGGCGGTACTGGA
GGAGGCGTATGCCAGCTGTAGTAATAGTTTGGCATCTGATATTTCCCCTCTGTGCTC
CACCTCTTTTGCCTGATTCATCCTTACCTATGTGTGGTCATGAACCACTCAGTAGCT
ACACCTCTGGTGGATTACAGAGAACGTATATCAAATAAAACCACATTGCAATAAAA
AAAAAAAAA (SEQ ID NO:254)

Translation:

MKLTCVVIIITVFLTLASQLITADYSRDQRQYRAVRLGDEMRFKRGARDCGGQGEGCYT
QPCCPGLRCRGGGTGGGVCQL (SEQ ID NO:255)

Toxin Sequence:

Asp-Cys-Gly-Gly-Gln-Gly-Xaa1-Gly-Cys-Xaa5-Thr-Gln-Xaa3-Cys-Cys-Xaa3-Gly-Leu-Arg-
Cys-Arg-Gly-Gly-Gly-Thr-Gly-Gly-Gly-Val-Cys-Gln-Leu-^ (SEQ ID NO:256)

Name: R6.9
Species: radiatus

Cloned: Yes

DNA Sequence:

ATCATGCAGAACTGACAATCCTGCTTCTTGTTGCTGCTATACTGATGTCGACCCAG
 5 GTCCTGATTCAAGGTGGTGGAGAAAAACGCCAAAAAGTCAACATTTTTTCAAAAAG
 AAAGACAGATGCTGAGACCTGGTGGGAGGGCGAATGCTCTAATTGGTTAGGAAGTT
 GTTCGACGCCCTCAAATTGCTGTCTCAAGAGTTGTAATGGGCACTGCACATTGTGGT
 GATGAACTCTGACCACAAAGCCATCCAACATCACCGCTCTCCTCTTCAGAGTCTTCA
 AG (SEQ ID NO:257)

Translation:

MQKLTIILLVAAILMSTQVLIQGGGEKRQKVNIFSKRKTD AETWWEGECSNWLGSCST
 PSNCCLKSCNGHCTLW (SEQ ID NO:258)

Toxin Sequence:

Xaa4-Xaa4-Xaa1-Gly-Xaa1-Cys-Ser-Asn-Xaa4-Leu-Gly-Ser-Cys-Ser-Thr-Xaa3-Ser-Asn-Cys-
 Cys-Leu-Lys-Ser-Cys-Asn-Gly-His-Cys-Thr-Leu-Xaa4-^ (SEQ ID NO:259)

Name: R6.10

Species: radiatus

Cloned: Yes

DNA Sequence:

ATCATGCAGAACTGATAATCCTGCTTCTTGTTGCTGCTGTACTGATGTCCACCCAG
 25 GCCCTGATTCAAGGTGGTGGAGGAAAACGCCAACAGGCAAAGAGCAAGTATTTTC
 CGAAAGAAAGGCACCTGCTAAGCGTTGGTTTGGACACGAAGAATGCACCTATTGGT
 TGGGGCCTTGTGAGGTGGACGACACGTGTTGTTCTGCCAGTTGTGAGTCCAAGTTCT
 GCGGGTTGTGGTGATGGACACTGACCACAAGTCATCCTACATCGCCACTCTCCTGTT
 CAGAGTCTTCAAG (SEQ ID NO:260)

Translation:

MQKLIIILLVAAVLMSTQALIQGGGGKRRQAKSKYFSEKAPAKRWFGHEECTYWLGP
 CEVDDTCCSASCESKFCGLW (SEQ ID NO:261)

Toxin Sequence:

Xaa4-Phe-Gly-His-Xaa1-Xaa1-Cys-Thr-Xaa5-Xaa4-Leu-Gly-Xaa3-Cys-Xaa1-Val-Asp-Asp-
 Thr-Cys-Cys-Ser-Ala-Ser-Cys-Xaa1-Ser-Lys-Phe-Cys-Gly-Leu-Xaa4-^ (SEQ ID NO:262)

Name: Wi6.1

Species: wittigi

Cloned: Yes

DNA Sequence:

GGATCCATGAAACTGACGTGTGTGGTGATCATCGCCTTGCTGTTTCCTGACGGCCTGT
 45 CAGCTCATTACGGCTGATTACTCCAGAGATGAGCAGTCTGGCAGTACAGTGCGGGTTT
 CTAGACAGACCACGGCGTTTTGGTTTCGTTTCATACCGTGCGCCCGTTTAGGTGAACCA

TGTACCATATGCTGCCGTCCTTTGAGGTGCCGTGAAAGCGGAACACCCACATGTCAA
GTGTGATTGTCTGGCATCTGATATTTCCCCTCTGTGCCCTACCCTCTTTTGCCTGAGT
CATCCATACCTGTGCTCGAG (SEQ ID NO:263)

5 **Translation:**

MKLTCVVIIALLFLTACQLITADYSRDEQSGSTVRFLDRPRRFGSFIPCARLGEPCTICCRP
LRCRESGTPTCQV (SEQ ID NO:264)

Toxin Sequence:

10 Phe-Gly-Ser-Phe-Ile-Xaa3-Cys-Ala-Arg-Leu-Gly-Xaa1-Xaa3-Cys-Thr-Ile-Cys-Cys-Arg-Xaa3-
Leu-Arg-Cys-Arg-Xaa1-Ser-Gly-Thr-Xaa3-Thr-Cys-Gln-Val-^ (SEQ ID NO:265)

Name: Rg6.6
Species: regius
Cloned: Yes

DNA Sequence:

GGATCCATGAAACTGACGTGCGTGGTGATCATGGCCTCGCTGTTCTGCGGCCTGT
CAATTCCTTACAGCTGGAGGTGACTCAAGAAGTAAGCAGCGGTATCCTGATTGGAG
GCTGGGCTACCGAAAGTCCAAGTTGATGGCTAAGAAGACGTGCCTGGAACATAACA
AACTATGTTGGTATGATAGAGACTGCTGCACCATATATTGTAATGAAAACAAATGC
GGCGTGAAACCTCAATGAATGTTTCACACACACACACACACACACACACACACACA
CACACACACACACACACACACACACACATCTGGCGTCTGACCATTCCCCCTCTGT
GCTCTATCCTCTTGTTCTGAGTCATCCATACCTGTGCTCGAG (SEQ ID NO:266)

Translation:

MKLTCVVIMASLFLAACQFLTAGGDSRSKQRYPDWRLGYRKSCLMAKKTCLHKNKLC
WYDRDCCTIYCNENKCGVKPQ (SEQ ID NO:267)

Toxin Sequence:

Thr-Cys-Leu-Xaa1-His-Asn-Lys-Leu-Cys-Xaa4-Xaa5-Asp-Arg-Asp-Cys-Cys-Thr-Ile-Xaa5-
Cys-Asn-Xaa1-Asn-Lys-Cys-Gly-Val-Lys-Xaa3-Gln-^ (SEQ ID NO:268)

Name: R6.9
Species: radiatus
Cloned: Yes

DNA Sequence:

ATCATGCAGAACTGACAATCCTGCTTCTTGTTGCTGCTATACTGATGTCGACCCAG
GTCCTGATTCAAGGTGGTGGAGAAAAACGCCAAAAAGTCAACATTTTTTCAAAAAG
AAAGACAGATGCTGAGACCTGGTGGGAGGGCGAATGCTCTAATTGGTTAGGAAGTT
GTTTCGACGCCCTCAAATTGCTGTCTCAAGAGTTGTAATGGGCACTGCACATTGTGGT
GATGAACTCTGACCACAAAGCCATCCAACATCACCGCTCTCCTCTTCAGAGTCTTCA
AG (SEQ ID NO:269)

Translation:

MQKLTIALLVAAILMSTQVLIQGGGEKRQKVNIFSKRKTD AETWWEGECSNWL GSCST
PSNCCLKSCNGHCTLW (SEQ ID NO:270)

5 **Toxin Sequence:**

Xaa4-Xaa4-Xaa1-Gly-Xaa1-Cys-Ser-Asn-Xaa4-Leu-Gly-Ser-Cys-Ser-Thr-Xaa3-Ser-Asn-Cys-
Cys-Leu-Lys-Ser-Cys-Asn-Gly-His-Cys-Thr-Leu-Xaa4-^ (SEQ ID NO:271)

10 **Name:** R6.10
Species: radiatus
Isolated: Yes
Cloned: Yes

15 **DNA Sequence:**

ATCATGCAGAACTGATAATCCTGCTTCTTGTTGCTGCTGTACTGATGTCCACCCAG
GCCCTGATTCAAGGTGGTGGAGGAAAACGCCAACAGGCAAAGAGCAAGTATTTTTC
CGAAAGAAAGGCACCTGCTAAGCGTTGGTTTGGACACGAAGAATGCACTTATTGGT
TGGGGCCTTGTGAGGTGGACGACACGTGTTGTTCTGCCAGTTGTGAGTCCAAGTTCT
20 GCGGGTTGTGGTGATGGACACTGACCACAAGTCATCCTACATCGCCACTCTCCTGTT
CAGAGTCTTCAAG (SEQ ID NO:272)

25 **Translation:**

MQKLIIALLVAAVLMSTQALIQGGGGKRQQA KSKYF SERKAPAKRWFGHEECTYWLGP
CEVDDTCCSASCESKFCGLW (SEQ ID NO:273)

30 **Toxin Sequence:**

Xaa4-Phe-Gly-His-Xaa1-Xaa1-Cys-Thr-Xaa5-Xaa4-Leu-Gly-Xaa3-Cys-Xaa1-Val-Asp-Asp-
Thr-Cys-Cys-Ser-Ala-Ser-Cys-Xaa1-Ser-Lys-Phe-Cys-Gly-Leu-Xaa4-^ (SEQ ID NO:274)

35 **Name:** Sf 5.1
Species: spurius
Cloned: Yes

40 **DNA Sequence:**

GGAAGCTGACTACAAGCAGAATGCGCTGTCTCCAGTCTTCGTCATTCTTCTGCTGC
TGATTCCATCTGCACCTAGCACTGATGCCCGACCGAAGACCAAAGATGATGTGCGC
CTGGCATCTTTCCACGGTAAGGCAAAGCGAACCCTACAAATACCTAGGGGGAATAT
40 CCACTGTTGCACAAAATATCAGCCGTGCTGTTCTTCACCATCATAAAGGGAAATGAC
TTTGATGAGACCCCTGCGAACTGTCCCTGGATGTGAAATTTGGAAACGAGACTGTTT
CTTTCGCGCGTGTTTCGTGGAATTTTGAATGGTCGTTAATAACACGCTGCCTCTTGCA
AACTACAATCTCTCTGTCCTTTATCTGTGGACTGGATGTCAACACTG (SEQ ID
NO:275)

45 **Translation:**

MRCLPVFVILLLLIPSAPSTDARPKTKDDVRLASFHGKAKRTLQIPRGNIHCCTKYQPCC
SSPS (SEQ ID NO:276)

Toxin Sequence:

5 Gly-Asn-Ile-His-Cys-Cys-Thr-Lys-Xaa5-Gln-Xaa3-Cys-Cys-Ser-Ser-Xaa3-Ser-^ (SEQ ID NO:277)

Name: Nb5.1

10 **Species:** nobilis

Cloned: Yes

DNA Sequence:

15 ATGCGCTGTCTCCCAGTCTTCGTCATTCTTCTGCTGCTGACTGCATCTGCACCAAGCG
TTGATGCCCCGACCGAAGACCAAAGATGATGTGCTCCGGGCATCTTTCCGCGATAAT
GCAAAGAGTACCCTACAAAGACTTTGGAACAAACGCATCTGCTGCCCCATAATTCTT
TGGTGCTGTGGTTAACCAGCATGAAGTTCCCAGGA (SEQ ID NO:278)

Translation:

20 MRCLPVFVILLLLTASAPSVDDARPKTKDDVLRASFRDNAKSTLQRLWNKRICCPHILWCC
G (SEQ ID NO:279)

Toxin Sequence:

25 Ile-Cys-Cys-Xaa3-Ile-Ile-Leu-Xaa4-Cys-Cys-# (SEQ ID NO:280)

Name: Bt5.1

Species: betulinus

Cloned: Yes

DNA Sequence:

30 ATGCGCTGTCTCCCAGTCTTCATCATTCTTCTGGTGCTGATTGCATCTGCACCTACCG
TTGATGCCCCGACCAAAGATCGAAGATGATGAGTCCCTGGCATCTTTCCATGNTCATN
AACCACCATNANNGTNCANCTTTTGAACAAACGCAATTGCTGCCCAGACTCTCCTC
35 CGTGCTGTCATTAACCAGCATGAAGGTTTCAGGA (SEQ ID NO:281)

Translation:

40 MRCLPVFIILLVLIASAPTVDARPKIEDDESASFH?H?PP????LLNKRNCCPDSPPCCH
(SEQ ID NO:282)

Toxin Sequence:

Asn-Cys-Cys-Xaa3-Asp-Ser-Xaa3-Xaa3-Cys-Cys-His-^ (SEQ ID NO:283)

45 **Name:** t-PVA

Species: purpurascens

Isolated: Yes

Cloned: Yes

DNA Sequence:

5 GGAATTCCAAATGATGTAATTACTGACTACATGGTCATAGTGTATACCCATTGAAAA
 ATTTCTATGACATTTTCAGTTGTTAGATCATCCAGTTCCACAGATGGAAAGACAGAGA
 GATAGTAGCTTGCAAGTGGCAGCGTGTGTTAACGACCATTTCGACATTCCATGAACA
 CGTGTGAAAGGAGCAGTCTGCTTTCCAAATCTGACATCCAGGGACAGTTTGCAGGG
 GTCTCATCCAAAGTCATCTTCTTTATCCCAAAGTACAGCACCGCATCTGTTTTGGA
 CAGCAACCGCGTTTCTTCCAAAATCTTTGTAGGGTTCCTTTTGCATTATCGTGGA
 10 GATGCCAGGGGCATATCATCTTTGGTCTTCGGATGAGCATCAACGCAAGGTGCAGA
 TGGAATCAGCAGCAGAAGAATGACGAAGACTGGCAGACAGCGCATTCTGCTTGTAG
 TCAGCTTCCGAATTCCAAGCCGAATTCTGCAGATATCCATCACACTGGCGGCCGCTC
 GAGCATGCATCTAGAGGGCCCAATTCGCCCTATAGTGAGTCGTATGACAATTCAcTG
 GC (SEQ ID NO:284)

Translation:

MRCLPVFVILLLLIPSAPCVDAHPKTKDDMPLASFHDNAKGTQLQRFWKKRGCCPKQMR
 CCTLG (SEQ ID NO:285)

Toxin Sequence:

Gly-Cys-Cys-Xaa3-Lys-Gln-Met-Arg-Cys-Cys-Thr-Leu-# (SEQ ID NO:286)

Name: Af5.2

Species: ammiralis

Cloned: Yes

DNA Sequence:

30 GGAAGCTGACTACAAGCAGAATGCACTGTCTCCAGTCGTCGTCATTCTTCTGCTGC
 TGA CTGCATCTGGTGGACCTAGCGTTGATGCCC GACTGAAGACCAAAGATGATGTG
 CCCCTGTCATCTTTCCGCGATAATACAAAGAGTATCCTACAAAGACTTTGGAAGCGA
 GGCAACTGCTGTGAATTTTGGGAGTTTGTCTGTGATTAACCAGCATGAAGG (SEQ ID
 NO:287)

Translation:

MHCLPVVVILLLLTASGGPSVDARLKT KDDVPLSSFRDNTKSILQRLWKRGNCCFEWFEF
 CCD (SEQ ID NO:288)

Toxin Sequence:

40 Gly-Asn-Cys-Cys-Xaa1-Phe-Xaa4-Xaa1-Phe-Cys-Cys-Asp-^ (SEQ ID NO:289)

Name: Da5.1

Species: dalli

45 **Cloned:** Yes

DNA Sequence:

GGAAGCTGACTACAAGCAGAATGCACTGTCTCCCAGTCTTCGTCATTCTTCTGCTGC
 TGACTGCATCTGGACCTAGCGTTGATGCCCAACCGAAGACCGAAGTTGATGTGCCC
 CTGTCATCTTTCCGCGATAATGCAAAGCGTGCCCTACAAAGACTTCCGCGTTGCTGT
 GAATATTGGAAGTTGTGCTGTGGTTAACCAGCATGAAGG (SEQ ID NO:290)

5

Translation:

MHCLPVFVILLLLTASGPSVDAQPKTEVDVPLSSFRDNAKRALQRLPRCCEYWKLC CG
 (SEQ ID NO:291)

10

Toxin Sequence:

Cys-Cys-Xaa1-Xaa5-Xaa4-Lys-Leu-Cys-Cys-# (SEQ ID NO:292)

Name: Om5.1
Species: omaria
Cloned: Yes

DNA Sequence:

GGAAGCTGACTACAAGCAGAATGCGCTGTCTCCCAGTCTTCGTCATTCTTCTGCTGC
 TAACTGCATCTGCACCTAGCGTTGATGCCCGACCGAAGGCCAAAGATGATGTGCCC
 CTGGCATCTTTCCGTGATAATGCAAAGAGTACCCTACAAAGACTTCAGGACAAACG
 CGTTTGCTGTGGCTATAAGTTTTTTTGTGCTGTCGTTAACCAGCATGAAGG (SEQ ID
 NO:293)

Translation:

MRCLPVFVILLLLTASAPSV DARPKAKDDVPLASFRDNAKSTLQRLQDKRVCCGYKFFC
 CR (SEQ ID NO:294)

Toxin Sequence:

Val-Cys-Cys-Gly-Xaa5-Lys-Phe-Phe-Cys-Cys-Arg-^ (SEQ ID NO:295)

Name: Au5.1
Species: aulicus
Cloned: Yes

DNA Sequence:

GGAAGCTGACTACAAGCAGAATGCGCTGTCTCCCAGTCTTCGTCATTCTTCTGCTGC
 TGACTGCATCTGCACCTAACGTTGATGCCCAACCGAAGACCAAAGATGATGTGCCC
 CTGGCATCTTTGCACGATGATGCAAAGAGTGCACTACAACATTGGAACCAACGCTG
 CTGCCCCATGATCTATTGGTGCTGTAGTTAACCAGCATGAAGG (SEQ ID NO:296)

Translation:

MRCLPVFVILLLLTASAPNVDAQPKTKDDVPLASLHDDAKSALQHWNQRCCPMIYWC
 CS (SEQ ID NO:297)

Toxin Sequence:

Cys-Cys-Xaa3-Met-Ile-Xaa5-Xaa4-Cys-Cys-Ser-^ (SEQ ID NO:298)

Name: Au5.4
Species: aulicus
Cloned: Yes

DNA Sequence:

GGAAGCTGACTACAAGCAGAATGCACTGTCTCCCAGTCTTCGTCATTCTTCTGCTGC
 TGACTGCATCTGCACCTAACGTTGATGCCCAACCGAAGACCAAAGATGATGTGCCC
 CTGGCATCTTTGCACGATGATGCAAAGAGTGCCTACAACATTGGAACCAACGCTG
 CTGCCCCGAGATCTATTGGTGCTGTAGTTAACCAGCATGAAGG (SEQ ID NO:299)

Translation:

MHCLPVFVILLLLTASAPNVDAQPKTKDDVPLASLHDDAKSALQHWNQRCCPEIYWCC
 S (SEQ ID NO:300)

Toxin Sequence:

Cys-Cys-Xaa3-Xaa1-Ile-Xaa5-Xaa4-Cys-Cys-Ser-^ (SEQ ID NO:301)

Name: Af5.1
Species: ammimalis
Cloned: Yes

DNA Sequence:

GGAAGCTGACTACAAGCAGAATGCGCTGTCTCCCAGTCTTCGTCATTCTTCTGCTGC
 TGATTGCATCTGCACCTAGCGTTGATGCCCAACCGAAGACCAAAGATGATGTGTCCC
 TGGCATCTTTGCACGATAATATAAAGAGTACTCTACAAACACTTTGGAACAAACGCT
 GCTGCCCCCCTGTGATTGTTGGTGCTGTGGTTAACCAGCATAAAGG (SEQ ID NO:302)

Translation:

MRCLPVFVILLLLIASAPSVDAQPKTKDDVSLASLHDNIKSTLQTLWNKRCCPPVIWCCG
 (SEQ ID NO:303)

Toxin Sequence:

Cys-Cys-Xaa3-Xaa3-Val-Ile-Xaa4-Cys-Cys-# (SEQ ID NO:304)

Name: Au5.3
Species: aulicus
Cloned: Yes

DNA Sequence:

GGAAGCTGACTACAAGCAGAATGCGCTGTCTCCCAGTCTTCGTCATTCTTCTGCTGC
 TGACTGCATCTGGACCTAGCGTTGATGCCCGACCGAAGACCAAAGATGATGTGCCT

CTGTCATCTTTCCGCGATAACGCAAAGAGTATCCTACAAAGACGTTGGAACAACCTAT
TGCTGCACGAATGAGCTTTGGTGCTGTGGTTAACCAGCATGAAGG (SEQ ID NO:305)

Translation:

5 MRCLPVFVILLLLTASGPSVDARPKTKDDVPLSSFRDNAKSILQRRWNNYCCTNELWCC
G (SEQ ID NO:306)

Toxin Sequence:

10 Xaa4-Asn-Asn-Xaa5-Cys-Cys-Thr-Asn-Xaa1-Leu-Xaa4-Cys-Cys-# (SEQ ID NO:307)

Name: Da5.2
Species: dalli
Cloned: Yes

DNA Sequence:

15 GGAAGCTGACTACAAGCAGAATGCACTGTCTCCAGTCTTCGTCATTCTTCTGCTGC
TGACTGCATCTGGACCTAGCGTTGATGCCCCGACCGAAGACCGAAGATGATGTGCCC
CTGTCATCTTTCCGCGATAATAACAAAGAGTACCCTACAAAGACTTTTGAAGCCAGTC
20 AACTGCTGTCCTATTGATCAATCTTGCTGTTCTTAACCAGCATGAAGG (SEQ ID
NO:308)

Translation:

25 MHCLPVFVILLLLTASGPSVDARPKTEDDVPLSSFRDNTKSTLQRLKPVNCCPIDQSCC
S (SEQ ID NO:309)

Toxin Sequence:

Xaa3-Val-Asn-Cys-Cys-Xaa3-Ile-Asp-Gln-Ser-Cys-Cys-Ser-^ (SEQ ID NO:310)

30 **Name:** Cn10.3
Species: consors
Cloned: Yes

DNA Sequence:

35 GGATCCATGTTACCGTGTTTCTGTTGGTTGTCTTGGCAACCACTGTCGTTTCCATCC
CTTCAGATCGTGCATCTGAAGGCAGGAATGCCGTAGTCCACGAGAGAGCGCCTGAG
CTGGTCGTTACGGCCACCACGACTTGCTGTGGTTATGATCCGATGACAATATGCCCT
40 CCTTGCATGTGCACTCATTCTGTCCACCAAAAAGAAAACCAGGCCGCAGAAACGA
CTGATGCTCGAG (SEQ ID NO:311)

Translation:

45 MFTVFLLVVLATTVVSI PSDRASEGRNAV VHERAPELVVTATTTCCGYDPMTICPPCMC
THSCPPKRKPGRND (SEQ ID NO:312)

Toxin Sequence:

Ala-Xaa3-Xaa1-Leu-Val-Val-Thr-Ala-Thr-Thr-Thr-Cys-Cys-Gly-Xaa5-Asp-Xaa3-Met-Thr-Ile-Cys-Xaa3-Xaa3-Cys-Met-Cys-Thr-His-Ser-Cys-Xaa3-Xaa3-Lys-Arg-Lys-Xaa3-# (SEQ ID NO:313)

5

Name: A10.2
Species: aurisiacus
Cloned: Yes

10

DNA Sequence:

GGATCCATGTTACCGTGTTTCTGTTGGTTGTCTTGGCAACCACTGTCGTTTCCATCC
 CTTTCAGATCGTGCATCTGATGGCAGGAATGCCGCAGTCAACGAGAGACAATCTTGG
 CTGGTCCCTTCGACAATCACGACTTGCTGTGGATATGATCCGGGGACAATGTGCCCT
 CCTTGCAGGTGCAATAATACCTGTAAACCAAAAAACCAAAACCAGGAAAAGGCC
 GCAGAAACGACTGATGCTCCAGGACCCTCTGAACCACGACCTCGAG (SEQ ID NO:314)

Translation:

MFTVFLLVVLATTVVVSIPSDRASDGRNAAVNERQSWLVPSTITTCCGYDPGTMCPPCRC
 NNTCKPKKPKPGKGRRND (SEQ ID NO:315)

Toxin Sequence:

Xaa2-Ser-Xaa4-Leu-Val-Xaa3-Ser-Thr-Ile-Thr-Thr-Cys-Cys-Gly-Xaa5-Asp-Xaa3-Gly-Thr-Met-Cys-Xaa3-Xaa3-Cys-Arg-Cys-Asn-Asn-Thr-Cys-Lys-Xaa3-Lys-Lys-Xaa3-Lys-Xaa3-Gly-Lys-# (SEQ ID NO:316)

30

Name: Cn10.4
Species: consors
Cloned: Yes

DNA Sequence:

GGATCCATGTTACCGTGTTTCTGTTGGTTGTCTTGGCAACCACTGTCGTTTCCATCC
 CTTTCAGATCGTGCATCTGATGGCAGGAATGCCGTAGTCCACGAGAGAGCGCCTGAG
 CTGGTCGTTACGGCCACCACGACTTGCTGTGGTTATGATCCGATGACATGGTGCCCT
 TCTTGCATGTGCACTTATTCCTGTCCCCACCAAAGGAAAAAACAGGCCGCAGAAA
 CGACTGATGCTCCAGGACCCTCTGAACCACGACCTCGAG (SEQ ID NO:317)

40

Translation:

MFTVFLLVVLATTVVVSIPSDRASDGRNAVVHERAPELVVTATTTCCGYDPMTWCPSCM
 CTYSCPHQRKKPGRRND (SEQ ID NO:318)

Toxin Sequence:

Ala-Xaa3-Xaa1-Leu-Val-Val-Thr-Ala-Thr-Thr-Thr-Cys-Cys-Gly-Xaa5-Asp-Xaa3-Met-Thr-Xaa4-Cys-Xaa3-Ser-Cys-Met-Cys-Thr-Xaa5-Ser-Cys-Xaa3-His-Gln-Arg-Lys-Lys-Xaa3-# (SEQ ID NO:319)

5 **Name:** M10.3
 Species: magus
 Cloned: Yes

DNA Sequence:

10 GGATCCATGTTACCGTGTTTCTGTTGGTTGTCTTGGCAACCAGTGTCGTTTCCATCC
 CTTCAGATCGTGCATCTGATGGCGGGAATGCCGTAGTCCACGAGAGAGCGCCTGAG
 CTGGTCGTTACGGCCACCACGACTTGCTGTGGTTATGATCCGATGACAATATGCCCT
 CCCTGCATGTGCACTCATTCTGTCCACCAAAAGGAAAACCAGGCCGCAGGAACGA
 CTGATGTCCAGGACCTCTGAACCACGACNCGAG (SEQ ID NO:320)

Translation:

15 MFTVFLLVVLATSVVSIPSDRASDGGNAVVHERAPELVVTATTTCCGYDPM TICPPCMC
 THSCPPKGKPGRRND (SEQ ID NO:321)

Toxin Sequence:

20 Ala-Xaa3-Xaa1-Leu-Val-Val-Thr-Ala-Thr-Thr-Thr-Cys-Cys-Gly-Xaa5-Asp-Xaa3-Met-Thr-Ile-
 Cys-Xaa3-Xaa3-Cys-Met-Cys-Thr-His-Ser-Cys-Xaa3-Xaa3-Lys-Gly-Lys-Xaa3-# (SEQ ID
 NO:322)

25 **Name:** A10.3
 Species: aurisiacus
 Cloned: Yes

DNA Sequence:

30 GAATTCGCCCTTGAGGATCCGTGTGGTTCTGGGTCCAGAACCTGATGGCAGGAATG
 CCGCAGTCAACGAGAGACAGAAATGGCTGGTCCATTGCGAAAATCACGTATTGCTGT
 GGTATAATAAGATGGACATGTGCCCTCCTTGCATGTGCACTTATTCCTGTCCCCC
 CTAAAAAAAAAAAGACCAGGCCGCAGAAACGACTGATGCTCCAGGACCCTCTGAA
 CCACGACCTCGAGCGAAGGGCGAATTC (SEQ ID NO:323)

Translation:

35 VVLGPEPDGRNAAVNERQKWLVHSKITYCCGYNKMDMCPPCMCTYSCPPLKKKRPGR
 RND (SEQ ID NO:324)

Toxin Sequence:

40 Xaa2-Lys-Xaa4-Leu-Val-His-Ser-Lys-Ile-Thr-Xaa5-Cys-Cys-Gly-Xaa5-Asn-Lys-Met-Asp-Met-
 Cys-Xaa3-Xaa3-Cys-Met-Cys-Thr-Xaa5-Ser-Cys-Xaa3-Xaa3-Leu-Lys-Lys-Lys-Arg-Xaa3-#
 (SEQ ID NO:325)

45 **Name:** A10.4
 Species: aurisiacus
 Cloned: Yes

DNA Sequence:

GAATTCGCCCTTGAGGATCCGTGTGGTTCTGGGTCCAGCATTTGATGGCAGGAATGC
 CGCAGTCAACGAGAGAGCGCCTTGGACGGTCGTTACGGCCACCACGAATTGCTGCG
 5 GTATTACCGGGCCAGGCTGCCTTCCTTGCCGTTGTACTCAAACATGTGGCTGATGCT
 CCAGGACCCTCTGAACCACGACCTCGAGCGAAGGGCGAATTC (SEQ ID NO:326)

Translation:

VVLGPAFDGRNAAVNERAPWTVVTATTNCCGITGPGCLPCRCTQTCG (SEQ ID
 10 NO:327)

Toxin Sequence:

Ala-Xaa3-Xaa4-Thr-Val-Val-Thr-Ala-Thr-Thr-Asn-Cys-Cys-Gly-Ile-Thr-Gly-Xaa3-Gly-Cys-
 Leu-Xaa3-Cys-Arg-Cys-Thr-Gln-Thr-Cys-# (SEQ ID NO:328)

Name: Mr1.3
 Species: marmoreus
 Cloned: Yes

DNA Sequence:

GGAAGCTGACTACAAGCAGAATGCGCTGTCTCCCAGTCTTGATCATTCTTCTGCTGC
 TGA CTGCATCTGCACCTGGCGTTGTTGTCTACCGAAGACCGAAGATGATGTGCCCA
 TGT CATCTGTCTACGGTAATGGAAAGAGTATCCTACGAGGGATTCTGAGGAACGGT
 25 GTTTGCTGTGGCTATAAGTTGTGCCTTCCATGTTAACCAGCATGAAGG (SEQ ID
 NO:329)

Translation:

MRCLPVLHLLLLTASAPGVVVLPKTEDDVPMSVYGNGKSILRGILRNGVCCGYKLCLP
 30 C (SEQ ID NO:330)

Toxin Sequence:

Asn-Gly-Val-Cys-Cys-Gly-Xaa5-Lys-Leu-Cys-Leu-Xaa3-Cys-^ (SEQ ID NO:331)

Name: Pn1.5
 Species: pennaceus
 Cloned: Yes

DNA Sequence:

GGAATTCGGAAGCTGACTACAAGCAGAATGCGCTGTCTCCCAGTCTTCGTCATTCTT
 CTGCTGCTGACTGCATCTGCACCTAGCGTTGATGCCAAAGTTCATCTGAAGACCAAA
 GGTGATGGGCCCCTGTCATCTTTCCGAGATAATGCAAAGAGTACCCTACAAAGACTT
 CAGGACAAAAGCACTTGCTGTGGCTTTAAGATGTGTATCCCTTGTAGTTAACCAGCA
 45 TGAAGGATCC (SEQ ID NO:332)

Translation:

MRCLPVFVILLLLTASAPSVDAKVHLKTKGDGPLSSFRDNAKSTLQRLQDKSTCCGFKM
CIPCS (SEQ ID NO:333)

Toxin Sequence:

5 Ser-Thr-Cys-Cys-Gly-Phe-Lys-Met-Cys-Ile-Xaa3-Cys-Ser-^ (SEQ ID NO:334)

Name: Pn1.6
Species: pennaceus
Cloned: Yes

DNA Sequence:

GAATTCGGAAGCTGACTACAAGCAGAATGCGTTGTCTCCCAGTCTTCGTCATTCTTC
TGCTGCTGACTGCATCTGGACCTAGCGTTGATGCCCCGACTGAAGACCAAAGATGAT
GTGCCCCCTGTCATCTTTCCGAGATAATGCAAAGAGTACCCTACAAAGACTTCAGGAC
AAACGCCTTTGCTGTGGCTTTTGGATGTGTATTCTTGTAATTAACCAGCATGAAGG
ATCC (SEQ ID NO:335)

Translation:

MRCLPVFVILLLLTASGPSVDARLKTDDVPLSSFRDNAKSTLQRLQDKRLCCGFWMCI
PCN (SEQ ID NO:336)

Toxin Sequence:

Leu-Cys-Cys-Gly-Phe-Xaa4-Met-Cys-Ile-Xaa3-Cys-Asn-^ (SEQ ID NO:337)

Name: Pn1.7
Species: pennaceus
Cloned: Yes

DNA Sequence:

GAATTCTCCCTTGGAATTCTGAAGCTGACTACAANCAGAATGCGTTGTCTCCCACTC
TTCGTCATTCTTCTGCTGCTGACTGCATCTGGACCTACTGTTGATGCCCCGACTGAAG
ACCAAAGATGATGTGCCCCCTGTCATCTTTCCGAGATAATGCAAAGAGTACCCTACA
AAGACTTCAGGACAAAAGCACTTGCTGTGGCTTTAAGATGTGTATTCTTGTTGTTA
ACCAGCATGAAGGATCC (SEQ ID NO:338)

Translation:

MRCLPLFVILLLLTASGPTVDARLKTDDVPLSSFRDNAKSTLQRLQDKSTCCGFKMCIP
CG (SEQ ID NO:339)

Toxin Sequence:

Ser-Thr-Cys-Cys-Gly-Phe-Lys-Met-Cys-Ile-Xaa3-Cys-# (SEQ ID NO:340)

Name: Ep1.5
Species: episcopatus

Cloned: Yes

DNA Sequence:

GAATTCGCCCTTGAATTTCGGAAGCTGACTACAAGCAGAATGCGCTGTCTCCCAGTC
 5 TTCGTCATTCTTCTGCTGCTGACTGCATCTGGACCTANTGTTGATGCCAAAGTTCATC
 TGAAGACCAAAGGTGATGGGCCCCTGTCATCTTCCGAGATAATGCAAAGAGTACC
 CTACAAAGACTTCAGGACAAAAGCACTTGCTGTGGCTATAGGATGTGTGTTCTTGT
 GGTAAACCAGCATGAAGGATCCV (SEQ ID NO:341)

Translation:

MRCLPVFVILLLLTASGPSVDAKVHLKTKGDGPLSSFRDNAKSTLQRLQDKSTCCGYR
 MCVPCG (SEQ ID NO:342)

Toxin Sequence:

15 Ser-Thr-Cys-Cys-Gly-Xaa5-Arg-Met-Cys-Val-Xaa3-Cys-# (SEQ ID NO:343)

Name: Mr1.1

Species: marmoreus

20 Isolated: Yes

Cloned: Yes

DNA Sequence:

GGCGAATACACCTGGCAGGTA CTCAACGAACTTCAGGACACATTCTTTTCACCTGGA
 25 CACTGGAAACTGACAACAGGCAGAATGCGCTGTCTCCCAGTCTTGATCATTCTTCTG
 CTGCTGACTGCATCTGCACCTGGCGTTGTTGTCTACCGAAGACCGAAGATGATGTG
 CCCATGTCATCTGTCTACGGTAATGGAAGAGTATCCTACGAGGAATTCTGAGGAA
 CGGTGTTTGCTGTGGCTATAAGTTGTGCCATCCATGTTAACCAGCATGAAGGGAAAT
 GACTTTGGATGAGACCCCTGCGAACTGTCCCTGGATGTGAAATTTGGAAAGCAGAC
 30 TGTTCTTTTCGCACGTATTCGTGGAATTTCAATGGTCGTAACAACACGCTGCCAC
 TTGCAGGCTACTATCTCTCTGTCTTTTCATCTGTGGAATGGATGATCTAACAACCTG
 AAATATCAGAAATTTTTCAATGGCTATACACTATGACCATGTAGTCAGTAATTATAT
 CATTTGGACCTTTTGAAATATTTTTCAATATGTAAAGTTTTTGCACCCTGGAAAGGTC
 TTTTGGAGTTAAATATTTTAGTATGTTATGTTTTGCATACAAGTTATAGAATGCTGTC
 35 TTTCTTTTGTTCACATCAATGGTGGGGGCAGAAATTATTTGTTTGGTCAATGTA
 ATTATGACCTGCATTTAGTGCTATAGTGATTGCATTTTCAGCGTGGAATGTTTAATCT
 GCAAACAGAAAGTGGTTGATCGACTAATAAAGATTTGCATGGCACAAAAAAAAAAAA
 AAAAAAGTACTCTGCGTTGTTACTCGAG (SEQ ID NO:344)

Translation:

MRCLPVLIIILLTASAPGVVVLPKTEDDVPMSVYGNKGSILRGILRNGVCCGYKLCHP
 C (SEQ ID NO:345)

Toxin Sequence:

45 Asn-Gly-Val-Cys-Cys-Gly-Xaa5-Lys-Leu-Cys-His-Xaa3-Cys-^ (SEQ ID NO:346)

Name: Mr1.2
Species: marmoreus
Isolated: Yes

5 **Toxin Sequence:**

Gly-Val-Cys-Cys-Gly-Xaa5-Lys-Leu-Cys-His-Xaa3-Cys-^ (SEQ ID NO:347)

10 **Name:** Bn1.5
Species: bandanus
Cloned: Yes

DNA Sequence:

ATGCGCTGTCTCCCAGTCTTGATCATTCTTCTGCTGCTGACTGCATCTGCACCTGGCG
 TTGATGTCCTACCGAAGACCGAAGATGATGTGCCCTGTCATCTGTCTACGATAATA
 CAAAGAGTATCCTACGAGGACTTCTGGACAAACGTGCTTGCTGTGGCTACAAGCTTT
 GCTCACCATGTTAACCAGCATGAAGGATCC (SEQ ID NO:348)

Translation:

MRCLPVLHLLLLTASAPGVDVLPKTEDDVPLSSVYDNTKSILRGLLDKRACCGYKLCSP
 C (SEQ ID NO:349)

Toxin Sequence:

Ala-Cys-Cys-Gly-Xaa5-Lys-Leu-Cys-Ser-Xaa3-Cys-^ (SEQ ID NO:350)

Name: Au1.4
Species: aulicus
Cloned: Yes

DNA Sequence:

GGAAGCTGACTACAAGCAGAATGCGCTGTCTCCCAGTCTTCGTCATTCTTCTGCTGC
 TGACTGCATCTGGACCTAGCGTTGATGCCCGACTGAAGACCAAAGATGATGTGCCC
 CTGTCATCTTTCCGAGATAATGCAAAGAGTACCCTACAAAGACATCAGGACAAAAG
 CGTTTGCTGTGGCTATAAGCTGTGTTTTCTTGTTGTTAACCAGCATGAAGG (SEQ ID
 NO:351)

Translation:

MRCLPVFVILLLLTASGPSVDARLKTDDVPLSSFRDNAKSTLQRHQDKSVCCGYKLCF
 PCG (SEQ ID NO:352)

Toxin Sequence:

Ser-Val-Cys-Cys-Gly-Xaa5-Lys-Leu-Cys-Phe-Xaa3-Cys-# (SEQ ID NO:353)

Name: Tx1.7
Species: textile

Cloned: Yes

DNA Sequence:

5 CAGGATCCAATGGGGTTTGTGTTGGCTATAGGATGTGTGTTTCCTTGTGGTTAACCAG
 CATGAAGGGAAATGACTTTGGATGAGACCCCTGCGAACTGTCCCTGGATGTGAGAT
 TTGGAAAGCAGACTGTTTCATTTTGCACGTGTTTCGTGGAATTCGAATGGTCGTTAAC
 AACACGCTGCCACTTGCAAGCTACTATCTCTCTGTCCTTTTATCTGTGGAACGTATG
 ATCTAACAACTGAAATATCATANANATTTTCAATGGGTATNCACTATGCATATGAT
 CATGTAGGGTTCAAGGGGTCAAGATNC (SEQ ID NO:354)

Translation:

GSNGVCCGYRMCVPCG (SEQ ID NO:355)

Toxin Sequence:

15 Asn-Gly-Val-Cys-Cys-Gly-Xaa5-Arg-Met-Cys-Val-Xaa3-Cys-# (SEQ ID NO:356)

Name: Tx1.6

Species: textile

Cloned: Yes

DNA Sequence:

25 ATGCACTGTCTCCCAATCTTCGTCATTCTTCTGCTGCTGACTGCATCTGGACCTAGCG
 TTGATGCCCAACTGAAGACCAAAGATGATGTGCCCTGTGCATCTTTCCGAGATCATG
 CAAAGAGTACCCTACGAAGACTTCAGGACAAACAGACTTGCTGTGGCTATAGGATG
 TGTGTTTCCTTGTGGTTAACCAGCATGAAGGATCC (SEQ ID NO:357)

Translation:

30 MHCLPIFVILLLLTASGPSVDAQLKTKDDVPLSSFRDHAKSTLRRLQDKQTCCGYRMCV
 PCG (SEQ ID NO:358)

Toxin Sequence:

Xaa2-Thr-Cys-Cys-Gly-Xaa5-Arg-Met-Cys-Val-Xaa3-Cys-# (SEQ ID NO:359)

Name: Afl.3

Species: ammimalis

Cloned: Yes

DNA Sequence:

40 AGAAGCTGACTACAAGCAGAATGCACTACCTCCCAGTCTTCGTCATTCTTCTGCTGC
 TGACTGCATCTGGACCTAGCGTTGATGCCCAACTGAAGACCAAAGATGATGTGCC
 CTGTCATCTTTCCGAGATAATGCAAAGAGTACCCTACGAAGACTCCAGTACAAACA
 GGCTTGCTGTGGCTTTAAGATGTGTGTTTCCTTGTGGTTAACCAGCATGAAGG (SEQ
 45 ID NO:360)

Translation:

MHYLPVVFVILLLLTASGPSVDAQLKTKDDVPLSSFRDNAKSTLRRRLQYKQACCGFKMC
VPCG (SEQ ID NO:361)

Toxin Sequence:

5 Xaa2-Ala-Cys-Cys-Gly-Phe-Lys-Met-Cys-Val-Xaa3-Cys-# (SEQ ID NO:362)

Name: Pn1.3
Species: pennaceus
Cloned: Yes

DNA Sequence:

ATGCGCTGTCTCCAGTCTTCGTCATTCTTCTGCTGCTGACTGCATCTGCACCTAGCG
TTGATGCCAAAGTTCATCTGAAGACCAAAGGTGATGGGCCCCTGTCATCTTTCCGAG
ATAATGCAAAGAGTACCCTACAAAGACTTCAGGACAAAAGCACTTGCTGTGGCTTT
AAGATGTGTATTCTTGTCGTTAACCAGCATGAAGGATCC (SEQ ID NO:363)

Translation:

MRCLPVFVILLLLTASAPSVDAKVHLKTKGDGPLSSFRDNAKSTLQRLQDKSTCCGFKM
CIPCR (SEQ ID NO:364)

Toxin Sequence:

Ser-Thr-Cys-Cys-Gly-Phe-Lys-Met-Cys-Ile-Xaa3-Cys-Arg-^ (SEQ ID NO:365)

Name: Pn1.4
Species: pennaceus
Cloned: Yes

DNA Sequence:

CAGGATCCAATGGGGTTTGTGTTGTGGCTTTTGGATGTGTATTCTTGTAATTAACCAG
CATGAAGGGAAATGACTTTGGATAAGACCCCTGCGAACTGTCCTTGGATGTGAGAT
TTGGAAAGCAGACTGTTCTTTTGCACGTGTTCTGTTGAATTCGAATGGTCGTTAAC
AACACGCTGCCACTTGCAAGCTACTATCTCTCTGTCCTTTCATCTGTGGAAGTGTATG
ATCTAACAACCTGAAATATCATAGAAATTTTCAATGGGTATACACTATGCATATGAC
CATGTANGGGTCAACAGNC (SEQ ID NO:366)

Translation:

GSNGVCCGFWMCIPCN (SEQ ID NO:367)

Toxin Sequence:

Asn-Gly-Val-Cys-Cys-Gly-Phe-Xaa4-Met-Cys-Ile-Xaa3-Cys-Asn-^ (SEQ ID NO:368)

Name: Om1.7
Species: omaria
Cloned: Yes

DNA Sequence:

GGAAGCTGACTACAAGCAGAATGCGCTGTCTCCCAGTCTTCGTCATTCTTCTGCTGC
 TGA CTGCATCTGCACCTAGCGTTGATGCCCCGACCGAAGGCCAAAGATGATGTGCCC
 5 CTGTCATCTTTCCGTGATAATGCAAAGAGTACCCTACAAAGACTTCAGGACAAAGA
 CGTTTGCTGTTACGTTAGAATGTGTCCTTGTCGTTAACCAGCATGAAGG (SEQ ID
 NO:369)

Translation:

10 MRCLPVFVILLLLTASAPSVDPKAKDDVPLSSFRDNAKSTLQRLQDKDVCCYVRMC
 PCR (SEQ ID NO:370)

Toxin Sequence:

Asp-Val-Cys-Cys-Xaa5-Val-Arg-Met-Cys-Xaa3-Cys-Arg-^ (SEQ ID NO:371)

Name: Conophysin-R
Species: radiatus
Isolated: Yes

Toxin Sequence:

His-Xaa3-Thr-Lys-Xaa3-Cys-Met-Xaa5-Cys-Ser-Phe-Gly-Gln-Cys-Val-Gly-Xaa3-His-Ile-Cys-
 Cys-Gly-Xaa3-Thr-Gly-Cys-Xaa1-Met-Gly-Thr-Ala-Xaa1-Ala-Asn-Met-Cys-Ser-Xaa1-Xaa1-
 Asp-Xaa1-Asp-Xaa3-Ile-Xaa3-Cys-Gln-Val-Phe-Gly-Ser-Asp-Cys-Ala-Leu-Asn-Asn-Xaa3-
 25 Asp-Asn-Ile-His-Gly-His-Cys-Val-Ala-Asp-Gly-Ile-Cys-Cys-Val-Asp-Asp-Thr-Cys-Thr-Thr-
 His-Leu-Gly-Cys-Leu-^ (SEQ ID NO:372)

Name: Ts10.1
Species: tessulatus
Cloned: Yes

DNA Sequence:

GGATCCATGTTACCGTGTTTCTGTTGGTTGTCTTGGCAACCACTGTTGTTTCCTTCA
 35 GTGCAGATCGTGCCAACGTCAAAGCGTCTGACCTGATCGCCCAGGCCACCAGAGAC
 GGCTGTCCACCACATCCCGTTCCTGGCATGCATAAGTGCATGTGTACTAATACATGT
 GGTTGAAGACGCTGATGCTCCAGGACCCTCTGAACCACGACCTCGAG (SEQ ID
 NO:373)

Translation:

40 MFTVFLLVVLATTVVVSFSADRANVKASDLIAQATRDGCPPHPVPGMHKCMCTNTCG
 (SEQ ID NO:374)

Toxin Sequence:

45 Asp-Gly-Cys-Xaa3-Xaa3-His-Xaa3-Val-Xaa3-Gly-Met-His-Lys-Cys-Met-Cys-Thr-Asn-Thr-
 Cys-# (SEQ ID NO:375)

Name: G1.4
Species: geographus
Cloned: Yes

DNA Sequence:

ANNTAGANTNTGTCGTANTANNGGATCNTAANTANTGNNTCGANATGATNANGAGT
 GATAAATGANNGGTGCACTNNTANTTANGNTNNTANGATNNNNATATTATNNTANN
 NNNTAANANATATNGGTNNGGANNAAGAAGANTAAAAGTANNGNTTNGTGAAANA
 ANGANNNNATGTTNNANNTCATAACNNNAATGTAAATAATANACGNNCCAGTGTG
 AAANNNTNTCNNNNATAAAAAATTCTNTNTNTNAANGTNNNTGTNTGNGTGTGTGTG
 TGTGTGTGTGTGTGTGNGTGTGTGTGNGTGTGTGTGTGTGTGTGTGTGTGTGNGTGT
 GTGTNTGTGNGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTNTGTGGTTCTGGGT
 CCAGCATCTGATGNCAGGGATGACACAGCCAAAGACGAAGGGTCTNACATGGACA
 AATTGGTCGAGAAAAAAGAATGTTGCCATCCTGCCTGTGGCAAACACTACAGTTGT
 GGACGCTGATGCTCCAGGGTNTGAAGGANCAA (SEQ ID NO:376)

Translation:

SDXRDDTAKDEGSXMDKLVEKKECCHPACGKHYSAGR (SEQ ID NO:377)

Toxin Sequence:

Xaa1-Cys-Cys-His-Xaa3-Ala-Cys-Gly-Lys-His-Xaa5-Ser-Cys-# (SEQ ID NO:378)

Name: G1.5
Species: geographus
Cloned: Yes

DNA Sequence:

GGATCCATGTTACCGTGTTTCTGTTGGTGGTCTTGGCAACCACTGTCGTTTCCTTCC
 CTTCAGAACGTGCATCTGATGGCAGGGATGACACAGCCAAAGACGAAGGGTCTGAC
 ATGGAGAAATTGGTCGAGAAAAAAGAATGTTGCAATCCTGCCTGTGGCAGACACTT
 CAGTTGTGGACGCTGATGCTCCAGGACCCTCTGAACCACGACTCGAG (SEQ ID
 NO:379)

Translation:

MFTVFLLVVLATTVVVSFPSEASDGRDDTAKDEGSDMEKLVEKKECCNPACGRHFSCG
 R (SEQ ID NO:380)

Toxin Sequence:

Xaa1-Cys-Cys-Asn-Xaa3-Ala-Cys-Gly-Arg-His-Phe-Ser-Cys-# (SEQ ID NO:381)

Name: S1.8
Species: striatus
Cloned: Yes

DNA Sequence:

GGATCCATGTTACACCGTGTTTCTGTTGGTTGTCTTGGCAACCACTGTCGTTTCCTTCA
 CTTTCAGATCGTGCATCTGATGGCAGGGATGACGAAGCCAAAGACGAAAGGTCTGAC
 5 ATGCACGAATCGGACCGGAAAGGACGCGCATACTGTTGCCATCCTGCCTGTGGCCC
 AAACCTATAGTTGTGGCACCTCATGCTCCAGGACCCTCTGAACCACGACCTCGAG
 (SEQ ID NO:382)

Translation:

10 MFTVFLLVVLATTVVVSFTSDRASDGRDDEAKDERSDMHESDRKGRAYCCHPACGPNY
 SCGTSCSRTL (SEQ ID NO:383)

Toxin Sequence:

Ala-Xaa5-Cys-Cys-His-Xaa3-Ala-Cys-Gly-Xaa3-Asn-Xaa5-Ser-Cys-Gly-Thr-Ser-Cys-Ser-Arg-
 5 Thr-Leu-^ (SEQ ID NO:384)

Name: S1.9

Species: striatus

Cloned: Yes

DNA Sequence:

GGATCCATGTTACACCGTGTTTCTGTTGGTTGTCTTGGCAACCACTGTCGTTTCCTTCA
 CTTTCAGATCGTGCATCTGATGGCAGGGATGACGAAGCCAAAGACGAAAGGTCTGAC
 25 ATGCACGAATCGGACCGGAAAGGACGCGCATACTGTTGCCATCCTGTCTGTGGCAA
 AAACCTTTGATTGTGGACGCTGATGCTCCAGGACCCTCTGAACCACGACCTCGAG
 (SEQ ID NO:385)

Translation:

30 MFTVFLLVVLATTVVVSFTSDRASDGRDDEAKDERSDMHESDRKGRAYCCHPVCGKNF
 DCGR (SEQ ID NO:386)

Toxin Sequence:

Ala-Xaa5-Cys-Cys-His-Xaa3-Val-Cys-Gly-Lys-Asn-Phe-Asp-Cys-# (SEQ ID NO:387)

Name: Ra1.1

Species: rattus

Cloned: Yes

DNA Sequence:

GGATCCATGTTACACCGTGTTTCTGTTGGTTGTCTTGGCAACCACTGTCGTTTCCTTCC
 CTTTCAGATCGTGCATCTGATGGCAGGGATGACGAAGCCAAAGACGAAAGGTCTGAC
 45 ATGCACGAATCGGACCGGAATGGACGCGGATGCTGTTGCAATCCTGCCTGTGGCCC
 AAACCTATGGTTGTGGCACCTCATGCTCCAGGACCCTCTGAACCACGACCTCGAG
 (SEQ ID NO:388)

Translation:

MFTVFLLVVLATTVVSFPSDRASDGRDDEAKDERSDMHESDRNGRGGCCNPACGPNY
GCGTSCSRTL (SEQ ID NO:389)

Toxin Sequence:

Gly-Cys-Cys-Cys-Asn-Xaa3-Ala-Cys-Gly-Xaa3-Asn-Xaa5-Gly-Cys-Gly-Thr-Ser-Cys-Ser-Arg-
Thr-Leu-^ (SEQ ID NO:390)

Name: Ar1.1
Species: arenatus
Cloned: Yes

DNA Sequence:

GGATCCATGTTACCGTGTTTCTGTTGGTTGTCTTGGCAACCACTGTGGATTCCTTCA
CTCCAGTTCGTA CTCTGTTGGCAGGAGTGCTGCAGCCAACGCGTTTGACCGGATCG
CTCTGACCGCCAGGCAAGATTATTGCTGTACCATTCCCAGCTGTTGGGATCGCTATA
AAGAGAGATGTAGACACATACGCTGATGCTCCAGGACCCTCTGAACCACGACCTTG
AG (SEQ ID NO:391)

Translation:

MFTVFLLVVLATTVDSTPVRTSVGRSAAANAFDRIALTARQDYCCTIPSCWDRYKERC
RHIR (SEQ ID NO:392)

Toxin Sequence:

Xaa2-Asp-Xaa5-Cys-Cys-Thr-Ile-Xaa3-Ser-Cys-Xaa4-Asp-Arg-Xaa5-Lys-Xaa1-Arg-Cys-Arg-
His-Ile-Arg-^ (SEQ ID NO:393)

Name: Er1.1
Species: eburneus
Cloned: Yes

DNA Sequence:

GGATCCATGTTACCGTGTTTCTGTTGGTTGTCTTGGCAACCACTGTGGATTCCTTCA
CTTCAGTTCGTA CTCTGTTGGCAGGAGTGCTGCAGCCAACGCGTTTGACCGGATCG
CTCTGACCGCCAGGCAAGATTATTGCTGTACCATTCCCAGCTGTTGGGATCGCTATA
AAGAGAGATGTAGACACATACGCTGATGCTCCAGGACCCTCTGAACCACGACCTCG
AG (SEQ ID NO:394)

Translation:

MFTVFLLVVLATTVDSTSVRTSVGRSAAANAFDRIALTARQDYCCTIPSCWDRYKERC
RHIR (SEQ ID NO:395)

Toxin Sequence:

Xaa2-Asp-Xaa5-Cys-Cys-Thr-Ile-Xaa3-Ser-Cys-Xaa4-Asp-Arg-Xaa5-Lys-Xaa1-Arg-Cys-Arg-His-Ile-Arg-^ (SEQ ID NO:396)

5 **Name:** Mi1.2
Species: miles
Cloned: Yes

DNA Sequence:

10 GGATCCATGTTACACCGTGTTTCTGTTGGTTGTCTTGGCAACTGCTGTTCTTCCAGTCA
 CTTTAGATCGTGCATCTGATGGAAGGAATGCAGCAGCCAACGCCAAAACGCCTCGC
 CTGATCGCGCCATTTCATCAGGGATTATTGCTGTCATAGAGGTCCCTGTATGGTATGG
 TGTGGTTGAAGCCGCTGCTGCTCCAGGACCCTCTGAACCACGACCTCGAG (SEQ ID
 NO:397)

Translation:

MFTVFLLVVLATAVLPVTLDRASDGRNAAANAKTPRLIAPFIRDYCCHRGPCMVWCG
 (SEQ ID NO:398)

Toxin Sequence:

Asp-Xaa5-Cys-Cys-His-Arg-Gly-Xaa3-Cys-Met-Val-Xaa4-Cys-# (SEQ ID NO:399)

Name: Jp1.1
Species: jaspedius
Cloned: Yes

DNA Sequence:

30 GGATCCATGTTACACCGTGTTTCTGTTGGTTGTCTTGGCAACCACTGTCGTTTCCA
 ACTCTTCAGATCGTGGTCCAGCATCTAATAAAAGGAAGAATGCCGCAATGCTTGACATG
 ATCGCTCAACACGCCATAAGGGGTTGCTGTTCCGATCCTCGCTGTAGATATAGATGT
 CGTTGAAGACGCTGCTGCTCCAGGACCCTCTGAACCACGACCTCGAG (SEQ ID
 NO:400)

Translation:

MFTVFLLVVLATTVVSNSSDRGPASNKRKNAAMLDMIAQHAIRGCCSDPRCRYRCR
 (SEQ ID NO:401)

Toxin Sequence:

40 Gly-Cys-Cys-Ser-Asp-Xaa3-Arg-Cys-Arg-Xaa5-Arg-Cys-Arg-^ (SEQ ID NO:402)

Name: a-OmIA
Species: omaria
Isolated: Yes

Toxin Sequence:

Gly-Cys-Cys-Ser-His-Xaa3-Ala-Cys-Asn-Val-Asn-Asn-Xaa3-His-Ile-Cys-Gly-# (SEQ ID NO:403)

5 **Name:** a-OmIA [COOH]
Species: omaria
Cloned: No

Toxin Sequence:

10 Gly-Cys-Cys-Ser-His-Xaa3-Ala-Cys-Asn-Val-Asn-Asn-Xaa3-His-Ile-Cys-Gly-^ (SEQ ID NO:404)

Name: Qc1.1
Species: quercinus
Cloned: Yes

DNA Sequence:

GGATCCATGTTACCGTGTTTCTGTTGGTTGTCTTGGCAACCACTGTCACTTCAGATC
 GTGTATCTAATGGCAGGAAAGCTGCAGCCAAATTCAAAGCGCCTGCCCTGATGGAG
 CTGTCCGTCAGGCAAGGATGCTGTTTCAGATCCTGCCTGTGCCGTGAGCAATCCAGAC
 ATCTGTGGCGGAGGACGCTGATGCTCCAGGACCCTCTGAACCACGACCTCGAG (SEQ ID NO:405)

Translation:

MFTVFLLVVLATTVTSDRVSNRKA AAKFKAPALMELSVRQGCCSDPACAVSNPDICG
 GGR (SEQ ID NO:406)

Toxin Sequence:

30 Xaa2-Gly-Cys-Cys-Ser-Asp-Xaa3-Ala-Cys-Ala-Val-Ser-Asn-Xaa3-Asp-Ile-Cys-Gly-Gly-#
 (SEQ ID NO:407)

Name: Bn1.6
Species: bandanus
Cloned: Yes

DNA Sequence:

GGATCCATGTTACCGTGTTTCTGTTGGTTGTCTTGGCAACCACTGTTGTTTCCTTCA
 CTTCAAATCGTGCATTTTCGTCTAGGAATGCCGTAGCCAAAGCGTCTGACCTGATCG
 CTCTGAACGCCAGGAGACCAGAATGCTGTACTCATCCTGCCTGTACGTGAGTCATC
 CAGAACTCTGTGGTTGAAGACGCTGACGCTCCAGGACCCTCTGAACCACGACCTCG
 AG (SEQ ID NO:408)

Translation:

MFTVFLLVVLATTVVSFTSNRAFRRRNAVAKASDLIALNARRPECCTHPACHVSHPELC
 G (SEQ ID NO:409)

Toxin Sequence:

Xaa3-Xaa1-Cys-Cys-Thr-His-Xaa3-Ala-Cys-His-Val-Ser-His-Xaa3-Xaa1-Leu-Cys-# (SEQ ID NO:410)

Name: Mr1.5
Species: marmoreus
Cloned: Yes

DNA Sequence:

GGATCCATGTTACCGTGTTTCTGTTGGTTGTCTTGGCAACCACTGTTGTTTCCTTCA
 CTTCAAATCGTGTTCTGGATCCAGCATTTCGTCTAGGAATGCCGCAGCCAAAGCGT
 CTGACCTGATCGCTCTGAACGCCAGGAGACCAGAATGCTGTACTCATCCTGCCTGTC
 ACGTGAGTAATCCAGAACTCTGTGGCTGAAGACGCTGATGCTCCAGGACCCTCTGA
 ACCACGACCTCGAG (SEQ ID NO:411)

Translation:

MFTVFLLVVLATTVVVSFTSNRVLDPAFRRRNAAKASDLIALNARRPECCTHPACHVSN
 PELCG (SEQ ID NO:412)

Toxin Sequence:

Xaa3-Xaa1-Cys-Cys-Thr-His-Xaa3-Ala-Cys-His-Val-Ser-Asn-Xaa3-Xaa1-Leu-Cys-# (SEQ ID NO:413)

Name: Mi1.1
Species: miles
Cloned: Yes

DNA Sequence:

GGATCCATGTTACCGTGTTTCTGTTGGTTGTCTTGGCAACCACTGTCGTTTCCGTCA
 CTTTCATATCGTGCATCTCATGGCAGGAAGGACGCAGCCGACCTGAGCGCTCTGAAC
 GACAACAATAATTGCTGTAACCATCCTGCCTGTGCCGGGAAAAATTCAGATCTTTGT
 GGTTGAAGACGCTGCTGCTCCAGGACCCTCTGAACCACGACCTCGAG (SEQ ID NO:414)

Translation:

MFTVFLLVVLATTVVSVTSYRASHGRKDAADLSALNDNNNCCNHPACAGKNSDLG
 (SEQ ID NO:415)

Toxin Sequence:

Cys-Cys-Asn-His-Xaa3-Ala-Cys-Ala-Gly-Lys-Asn-Ser-Asp-Leu-Cys-# (SEQ ID NO:416)

Name: MII[YHT]
Species: magus

Toxin Sequence:

Gly-Cys-Cys-Xaa5-His-Xaa3-Thr-Cys-His-Leu-Xaa1-His-Ser-Asn-Leu-Cys-# (SEQ ID NO:417)

Name: Nb1.1
Species: nobilis
Cloned: Yes

DNA Sequence:

GGATCCATGTTACCGTGTTTCTGTTGGTTGTCTTGGCAACCACTGTTGTTTCCTTCA
 CTTCAGATCGTGCATCTGATGGCAGGAATGCCGCAGCCAAAGCTTCTGACCTGATTG
 CTTTGACCGTCAGGGGATGCTGTGAGCGACCTCCCTGTCGCTGGCAAAATCCAGATC
 TTTGTGGTGGAAGGCGCTGANATTCCAGGACCCTCTGAACCACGACCTCGAG (SEQ ID NO:418)

Translation:

MFTVFLLVVLATTVVVSFTSDRASDGRNAAAKASDLIALTVRGCCERPPCRWQNPDLGG
 RRR (SEQ ID NO:419)

Toxin Sequence:

Gly-Cys-Cys-Xaa1-Arg-Xaa3-Xaa3-Cys-Arg-Xaa4-Gln-Asn-Xaa3-Asp-Leu-Cys-Gly-# (SEQ ID NO:420)

Name: Ak1.1
Species: atlanticus
Cloned: Yes

DNA Sequence:

GGATCCATGTTACCGTGTTTCTGTTGGTTGTCTTGGCAACCACAGTCGTTTCCTTCA
 CTTCAGATAGTGCATTTGATAGCAGGAATGTGCGCAGCCAACGACAAAGTGTCTGAC
 ATGATCGCTCTGACCGCCAGGAGAACATGCTGTTCCCGTCCTACCTGTAGAATGGAA
 TATCCAGAACTTTGTGGTGGAAGACGCTGATACTCCAGGACCCTCTGAACCACGAC
 CTCGAG (SEQ ID NO:421)

Translation:

MFTVFLLVVLATTVVVSFTSDSAFDSRNVAANDKVSDMIALTARRTCCSRPTCRMYPEL
 CGGRR (SEQ ID NO:422)

Toxin Sequence:

Thr-Cys-Cys-Ser-Arg-Xaa3-Thr-Cys-Arg-Met-Xaa1-Xaa5-Xaa3-Xaa1-Leu-Cys-Gly-# (SEQ ID NO:423)

Name: Qc1.2

Species: quercinus
Cloned: Yes

DNA Sequence:

5 GGATCCATGTTACCGTGTTTCTGTTGGTTGTCTTGGCAATCACGGTGGTTTCCTTCA
 CCTCAGATCATGCATCTGATGGCAGGAATACCGCAGCCAACGACAAAGCGTCTAAA
 CTGATGGCTCTTACGAACGAATGCTGTGACAATCCTCCGTGCAAGTCGAGTAATCCA
 GATTTGTGTGACTGGAGAAGCTGATGCTCCAGGACCCTNTGAACCACGACCTCGAG
 (SEQ ID NO:424)

Translation:

MFTVFLLVLAITVVSFTSDHASDGRNTAANDKASKLMALTNECCDNPPCKSSNPDLCDWRS (SEQ ID NO:425)

Toxin Sequence:

Asn-Xaa1-Cys-Cys-Asp-Asn-Xaa3-Xaa3-Cys-Lys-Ser-Ser-Asn-Xaa3-Asp-Leu-Cys-Asp-Xaa4-Arg-Ser-^ (SEQ ID NO:426)

Name: Lp1.1
Species: leopardus
Cloned: Yes

DNA Sequence:

5 GGATCCATGTTACCGTGTTTCTGTTGGTTGTCTTGGCAACCACGGTCGTTTCCCTCA
 CTTTAGATCGTGCATCTGGTGGCAGGAGATCTGGAGCCGACAACATGATTGCTCTTC
 TGATCATCAGAAAATGCTGTTCCAATCCCGCCTGTAACAGGTATAATCCAGCAATTT
 GTGATTGAAGACGCTAATGCTCCAGGACCCTCTGAACCACGACCTCGAG (SEQ ID NO:427)

Translation:

MFTVFLLVVLATTVVSLTLDRASGGRRSGADNMIALLIIRKCCSNPACNRYNPAICD (SEQ ID NO:428)

Toxin Sequence:

Cys-Cys-Ser-Asn-Xaa3-Ala-Cys-Asn-Arg-Xaa5-Asn-Xaa3-Ala-Ile-Cys-Asp-^ (SEQ ID NO:429)

Name: Em1.1
Species: emaciatius
Cloned: Yes

DNA Sequence:

45 GGATCCATGTTACCGTGTTTCTGTTGGTTCTCTTGGCAACCACTGTCACTTTACATC
 GTGCATCTAATGGCAGGAATGCCGCAGCCAGCAGGAAAGCGTCTGCCCTGATCGCT
 CAGATCGCCGGTAGAGACTGCTGTAACCTTCCTGCTTGTGCCGCGAGTAATCCAGGC

CTTTGTACTTGAAGACGCTGCTGCTCCAGGACCCTCTGAACCACGACCTCGAG (SEQ ID NO:430)

Translation:

5 MFTVFLLVLLATTVTLHRASNGRNAAASRKASALIAQIAGRDCCNFPACAASNPGGLCT
(SEQ ID NO:431)

Toxin Sequence:

10 Asp-Cys-Cys-Asn-Phe-Xaa3-Ala-Cys-Ala-Ala-Ser-Asn-Xaa3-Gly-Leu-Cys-Thr-^ (SEQ ID NO:432)

Name: C. victor alpha

Species: victor

Cloned: Yes

DNA Sequence:

GGATCCATGTTACCGTGTTTCTGTTGGTTGTCTTGGCAACCACCATCGTTTCCTCCA
CTTTAGATCGTGCATCTGATGGCATGAATGCTGCAGCGTCTGACCTGATCGCTCTGA
GCATCAGGAGATGCTGTTCTTCTCCTCCCTGTTTCGCGAGTAATCCAGCTTGTGGTA
GACGACGCTGATGCTCCAGGACCCTCTGAACCACGACCTCGAG (SEQ ID NO:433)

Translation:

5 MFTVFLLVVLATTIVSSTLDRASDGMNAAASDLIALSIRRCCSSPPCFASNPACGRRR
(SEQ ID NO:434)

Toxin Sequence:

Cys-Cys-Ser-Ser-Xaa3-Xaa3-Cys-Phe-Ala-Ser-Asn-Xaa3-Ala-Cys-# (SEQ ID NO:435)

Name: Cj1.1

Species: cinereus gubba

Cloned: Yes

DNA Sequence:

35 GGATCCATGTTACCGTGTTTCTGTTGGTTGTCCTGGCAACCACTATCGTTTCCTCCA
CTTCAGGTCATGCATTTGATGGCAGGAATGCTGCAGCCGACTACAAAGGGTCTGAA
TTGCTTGCTATGACCGTCAGGGGAGGATGCTGTTTCCTTTCCTCCCTGTATCGCAAAT
AATCCTTTTTTGTGCTGGAAGACGCTGATGCTCCAGGACCCTCTGAACCACGACCTCG
40 AG (SEQ ID NO:436)

Translation:

45 MFTVFLLVVLATTIVSSTSGHAFDGRNAAADYKGSELLAMTVRGGCCSFPPCIANNPFC
AGRR (SEQ ID NO:437)

Toxin Sequence:

Gly-Gly-Cys-Cys-Ser-Phe-Xaa3-Xaa3-Cys-Ile-Ala-Asn-Asn-Xaa3-Phe-Cys-Ala-# (SEQ ID NO:438)

5 **Name:** Fd1.1
Species: flavidus
Cloned: Yes

DNA Sequence:

10 GGATCCATGTTACCGTGTTTCTGTTGGTTGTCTTCGCATCCTCTGTCACTTTAGATC
 GTGCATCTCATGGCAGGTATATCCCAGTCGTCGACAGAGCGTCTGCCCTGATGGCTC
 AGGCCGACCTTAGAGGTTGCTGTTCCAATCCTCCTTGTTTCCTATCTTAATCCAGCCTG
 TGGTTAAAGACGCTGCCGCTCCAGGACCCTCTGAACCACGACCTCGAG (SEQ ID NO:439)

Translation:

MFTVFLLVVFASSVTLDRA SHGRYIPVVDRA SALMAQADLRGCCSNPPCSYLN PACG
 (SEQ ID NO:440)

Toxin Sequence:

Gly-Cys-Cys-Ser-Asn-Xaa3-Xaa3-Cys-Ser-Xaa5-Leu-Asn-Xaa3-Ala-Cys-# (SEQ ID NO:441)

25 **Name:** Em1.2
Species: emaciatus
Cloned: Yes

DNA Sequence:

30 GGATCCATGTTACCGTGTTTCTGTTGGTTGTCTTCGCATCCTCTGTCACTTTAGATC
 GTGCATCTCATGGCAGGTATGCCGCAAGTCGTCAACAGAGCGTCTGCCCTGATGGCTC
 ATGCCGCCCTTCGAGATTGCTGTTCCGATCCTCCTTGCTGCTCATAATAATCCAGACT
 GTCGTTAAAGACGCTGCTGCTCCAGGACCCTCTGAACCACGACCTCGAG (SEQ ID NO:442)

Translation:

35 MFTVFLLVVFASSVTLDRA SHGRYAAVVNRASALMAHAALRDCCSDPPCAHNNPDCR
 (SEQ ID NO:443)

Toxin Sequence:

40 Asp-Cys-Cys-Ser-Asp-Xaa3-Xaa3-Cys-Ala-His-Asn-Asn-Xaa3-Asp-Cys-Arg-^ (SEQ ID NO:444)

45 **Name:** Gel1.1
Species: generalis
Cloned: Yes

DNA Sequence:

GGATCCATGTTACCGTGTTTCTGTTGGTTGTCTTGGCAACTACTGTCGTTTCCTTCA
 CTTCAGATCGTGGGTCTGATGGCAGGAATGCCGCAGCCAAGGACAAAGCGTCTGAC
 CTGGTCGCTCTGACCGTCAAGGGATGCTGTTCTAATCCTCCCTGTTACGCGAATAAT
 CAAGCCTATTGTAATGGAAGACGCTGATGCTCCAGGACCCTCTGAACCACGACCTC
 GAG (SEQ ID NO:445)

Translation:

MFTVFLLVVLATTVVVSFTSDRGSDGRNAAKDKASDLVALTVKGCCSNPPCYANNQA
 YCNGRR (SEQ ID NO:446)

Toxin Sequence:

Gly-Cys-Cys-Ser-Asn-Xaa3-Xaa3-Cys-Xaa5-Ala-Asn-Asn-Gln-Ala-Xaa5-Cys-Asn-# (SEQ ID NO:447)

Name: Wi1.1
Species: wittigi
Cloned: Yes

DNA Sequence:

GGATCCATGTTACCGTGTTTCTGTTGGTTGTCCTGGCAACCACTGTCGTTTCCCCCA
 CTAGAGATCGTGCATCTGGTGTGAGGAATGTTGTTGCAACAAGCTTTCAGACTCTGA
 CCCACGATGAATGCTGTGACACCCCTTCCTGTTGGAAGGCCGAAGACCTGATTTGTA
 CTAATCAACGTCGCAGGACCCTCTGAACCACGACCTCGAG (SEQ ID NO:448)

Translation:

MFTVFLLVVLATTVVSPTRDRASGVRNVVATSFQTLTHDECCAHPSCWKAEDLICTNQ
 RRRTL (SEQ ID NO:449)

Toxin Sequence:

Asp-Xaa1-Cys-Cys-Ala-His-Xaa3-Ser-Cys-Xaa4-Lys-Ala-Xaa1-Asp-Leu-Ile-Cys-Thr-Asn-Gln-
 Arg-Arg-Arg-Thr-Leu-^ (SEQ ID NO:450)

Name: Ca1.5
Species: characteristicus
Cloned: Yes

DNA Sequence:

GGATCCATGTTACCGTGTTTCTGTTGGTTGTCTTGGCAACCACTGTCGTTTCCTTCA
 CTTCAGATCGTGCCTCTGAAGGCAGGAATGCTGCAGCCAAGGACAAAGCGTCTGAC
 CTGGTGGCTCTGAGAGTCAGGGGATGCTGTGCCATTCTGTAATGTCGCTTGCAGAAT
 GCAGCGTATTGTGGTGAATATCCTGATGCTCCAGGACCCTCTGAACCACGACCTCG
 AG (SEQ ID NO:451)

Translation:

MFTVFLLVVLATTVVVSFTSDRASEGRNAAKDKASDLVALRVRGCCAIRECRLQNAAY
CGGIS (SEQ ID NO:452)

Toxin Sequence:

Gly-Cys-Cys-Ala-Ile-Arg-Xaa1-Cys-Arg-Leu-Gln-Asn-Ala-Ala-Xaa5-Cys-Gly-Gly-Ile-Ser-[^]
(SEQ ID NO:453)

Name: Bt1.10
Species: betulinus
Cloned: Yes

DNA Sequence:

AGTAATTNATATANNAGAAAGNAANANAAAANNATANAGAATTTAAGTAATNTAA
GAANNAGAGANAGTGAATAGNAGNTAAGTAGANNAAGANAGGTAGANAGNANANG
NGGANGNTAGNTAATAGATANNNTATNGAGANATTANTAGCNGTATANANAAGAA
AAGAGGGNAANNNGAAATGNNGNAANNATAANTANTANNNGATNGANNNGNAAGTG
NNAAGNGTANAAGGAANAACAAANTNGTTGTNTAATNTGNNTGNGTGTGTNTGTGT
GNGTGTGTGTGTGTGNGT
GTGTGNGT
TCCAGCATCTGGTGGCAGGAAGGCTGCAGCCAAAGCGTCTAACCGGATCGCTCTGA
CCGTCAGGAGTGCAACATGCTGTTATTATCCTCCCTGTTACGAGGCTTATCCAGAAA
GTTGTCTGTAACGTGAATCATCCAGACCTTTGTGGCTGAAGACCCTGATGCTCCAGG
GGCAAGTTCAA (SEQ ID NO:454)

Translation:

SGGRKAAAKASNRIALTVRSATCCYPPCYEAYPESCL (SEQ ID NO:455)

Toxin Sequence:

Ser-Ala-Thr-Cys-Cys-Xaa5-Xaa5-Xaa3-Xaa3-Cys-Xaa5-Xaa1-Ala-Xaa5-Xaa3-Xaa1-Ser-Cys-
Leu-[^] (SEQ ID NO:456)

Where:

Xaa1 is Glu or γ -carboxy-Glu

Xaa2 is Gln or pyro-Glu

Xaa3 is Pro or hydroxy-Pro

Xaa4 is Trp (D or L) or bromo-Trp (D or L)

Xaa5 is Tyr, ¹²⁵I-Tyr, mono-iodo-Tyr, di-iodo-Tyr, O-sulpho-Tyr or O-phospho-Tyr

[^] is free carboxyl or amidated C-terminus, preferably free carboxyl

is free carboxyl or amidated C-terminus, preferably amidated

? is free carboxyl or amidated C-terminus

TABLE 2

Alignment of γ -Conopeptides¹ (SEQ ID NO:)

4/43 SNX	-----DCRGYDAPCSSGAPCCDWWTCSARTNRCF^ (457)
Af6.1	GMW---GDCKDGLTTCTFAPSECCSE-DC-E-GS-CTMW^ (458)
5 Af6.2	---WREGSCTSWLATCTQDQCCTD-VCYKRDY-CALWDDR^ (459)
Af6.3	-----N---CSDDWQYCESPSDCCSW-DC-D-VV-CS# (460)
Af6.4	--WWRWGGCMAWFGKCSKSECCSN-SC-DITR-CELMRFPPDW^ (461)
Af6.5	-----DCRGYDAPCSSGAPCCDWWTCSARTGRCF^ (462)
Af6.6	---L---CPDYTEPCSHAHECCSW-NC-HNGH-CT# (463)
10 Af6.7	-----CSSWAKYCEVDSECCSE-QC-VRSY-CAMW^ (464)
g-PnVIIA	-----DCTSWFGRCTVNSXCCSN-SC-DQTY-CXLYAFOS^ ² (465)
Gm6.7	-----ECRAWYAPCSPGAQCCSLLMCSKATSRILAL^ ² (466)
J010	-----CKTYSKYCXADSXCTX-QC-VRSY-CTLF# ² (467)
Mr6.1	----N-GQCEDVWMPCTSNWXCCSL-DC-E-MY-CTQI# ² (468)
15 Mr6.2	-----CGGWSTYCEVDEXCCSE-SC-VRSY-CTLF# ² (469)
Mr6.3	----N-GGCKATWMSGSGWXCCSM-SC-D-MY-C# ² (470)
R6.10	--UFGHXXCTYULGPCXVDDTCCSA-SC-XSKF-CGLU^ (471)
R6.9	--WWE-GECSNWLGSCTPSNCCLK-SC-N-GH-CTLW^ (472)
Tx6.1	---L---CODYTXOC SHAHXCCSW-NC-YNGH-CT# ² (473)
20 Tx6.14	-----DCYSWLGSCLAPSQCCSE-VC-D-YY-CRLWR^ (474)
Tx6.4	--WL---ECSVWFSHCTKDSXCCSN-SC-DQTY-CTLMPPDW^ ² (475)
Tx6.5	GMW---GECKDGLTTCLAPSXCCSE-DC-E-GS-CTMW^ ² (476)
Tx6.6	D-WWD-DGCSV-WGPCTVNAXCCSG-DC-H-ET-CIFGWEV^ ² (477)
Tx6.9	--WWRWGGCMAWFLGCSRDSXCCSN-SC-DVTR-CELMFPFPDW^ ² (478)
25 TxVIIA	-----CGGYSTYCXVDSXCCSD-NC-VRSY-CTLF# (479)

¹ The E may be Glu or Gla, the P may be Pro or hydroxy-Pro, and W may be Trp or bromo-Trp.

² Peptide disclosed in U.S. Serial No. 09/210,952 (PCT/US98/26792).

TABLE 3

Alignment of σ -Conopeptides (SEQ ID NO:)

Ca8.1	GCS-GT-CHRRDGGK-RTGDCSG-YSYCRCG-DAHHFYRGCTCSCQ# (480)
Ca8.2	GCSG-T-CHRRDGGK-RTGDCSG-YSYCRCG-DAHHFYRGCTCTC^ (481)
35 Ca8.3	GCSG-T-CRRHRDGGK-RTGDCSG-YSYCRCG-DAHHFYRGCTCTC^ (482)
Ca8.4	GCSG-T-CRRHRDGGK-RTGDCSG-YSYCRCG-DAHHFYRGCTCTC^ (483)
Ca8.5	GCSG-T-CHRRDGGK-RTGDCSG-YSYCRCG-DAHHFYRGCTCTC^ (484)
Ca8.6	GCSG-T-CHRRQNGEC-QGTCDG-HDHCDG-DTLGTYSGVCIC^ (485)
La8.1	QSE--TACRSLGSYQCM-GKCQ-LGVHSWCECIYNRGSQKSGCACRCQK^ (486)
40 Mn8.1	QCTLVNCDNRNGERACN-GDCSCEGQI--CKCGYRVSPGKSGCACTCRNAK^ (487)
P8.1	GCS-GSPCFKNKT--C-RDECICGG-LSNCWCGY-GGS--RGCKTCRE^ (488)
R8.1	KCNF-DKCKGTGVYNGC-ESCSCEGLHS-CRCTYNIGSMKSGCACICTYY^ (489)
R8.2	YGLGCA-GT-CGSSSN--CVRDYCDC-P-KPNCYCT-GKGFRQPGCGCSCL# (490)
Sx8.1	QCTFVNQCQNG--CAN-GDCSCGDQI--CKCGYRISPGSGCACTCRNAK^ (491)
45 T8.1	FGPIC---T-CFKSQN--C-RGSCECMS-PPGCYCS-NNGIRERGCSTCPGT# (492)
T8.2	GCT--GNCDW----TCS-GDCSCQGTSDSCHCIPPKSIGNR-CRCQCKRKIEID^ (493)

TABLE 4Alignment of τ -Conopeptides (SEQ ID NO:)

	Tx5.2a	---ECCEDGW-CCTAAPLT# ¹ (494)
	Tx5.2b	---GCCEDGW-CCTAAPLT# ¹ (495)
5	Mr5.1	--NGCC-RAGDCCSRFEIKENDF# ¹ (496)
	Mr5.3	--NGCC-RAGDCCS ^{^1} (497)
	Mr5.2	--NACC-IVRQCC ^{^1} (498)
	Qc5.1	---GCCAR-LTCCV# ¹ (499)
	Qc5.2	---GCCAM-LTCCV# ¹ (500)
10	t-PVA	---GCCPKQMRCCCTL# ¹ (501)
	Ca5.1	----CCPRRLACCII# ¹ (502)
	Ca5.2	----CCPNK-PCCFI# ¹ (503)
	G5.1	-ZGWCCKENIACCI ^{^1} (504)
	G5.2	-ZGWCCKENIACCV ^{^1} (505)
15	Im5.1	DWNSCCGKNPGCCPW# ¹ (506)
	Bt5.1	---NCCPDSPPCCH [^] (507)
	Af5.2	--GNCCEFWEFCCD [^] (508)
	Da5.1	----CCEYWKLC# (509)
	Om5.1	---VCCGYKFFCCR [^] (510)
20	t-AuVA	---FCCPVIRYCCW ^{^1} (511)
	t-AuVB	---FCCPFIRYCCW ^{^1} (512)
	Au5.1	----CCPMIYWCCS [^] (513)
	Au5.4	----CCPEIYWCCS [^] (514)
	Nb5.1	---ICCPILWCC# (515)
25	Af5.1	----CCPPVIWCC# (516)
	Tx5.1	----CCQTFYWCCVQ# ¹ (517)
	Au5.3	WNNYCCTNELWCC# (518)
	Gm5.1	---LCCVTEDWCCEWW ^{^1} (519)
	Gm5.2	---VCCRPVQDCCS# ¹ (520)
30	Da5.2	-PVNCCPIDQSCCS [^] (521)
	Sf5.1	GNIHCCTKYQPCCSSPS [^] (522)

¹ Peptide disclosed in U.S. Serial No. 09/497,491 (PCT/US00/03021).TABLE 5Alignment of Mar-Type Conopeptides¹ (SEQ ID NO:)

	Tx1.6 (Q819)	-ZTCCGYRMCVPC# (523)
	Bn1.5 (Q818)	-A-CCGYKLCSPC [^] (524)
	Pn1.3 (Q820)	-STCCGFKMCIPCR [^] (525)
40	Pn1.5 (AA200)	-STCCGFKMCIPCS [^] (526)
	Pn1.7 (AA456)	-STCCGFKMCIPC# (527)
	Ep1.5 (AA457)	-STCCGYRMCVPC# (528)
	Mr1.3	NGVCCGYKLCLPC [^] (529)
	Pn1.6 (AA390)	--LCCGFWMCIPCN [^] (530)
45	Mr1.1	NGVCCGYKLCHOC [^] (531)

Mr1.2	-GVCCGYKLCHOC^ (532)
Bn1.5	--ACCGYKLCSPC^ (533)
Au1.4	-SVCCGYKLCFPC# (534)
Tx1.7	NGVCCGYRMCVPC# (535)
5 Tx1.6	-ZTCCGYRMCVPC# (536)
Af1.3	-ZACCGFKMCVPC# (537)
Pn1.3	-STCCGFKMCIPCR^ (538)
Pn1.4	NGVCCGFWMCIPCN^ (539)
Om1.7	-DVCCYVRMC-PCR^ (540)

¹ Some peptides disclosed in U.S. Serial No. 09/580,201. P may also be O and O may also be P.

TABLE 6

Alignment of Contryphans* (SEQ ID NO:)

Contryphan-Im	Z--C-GQAWC# (541)
Contryphan-Sm-dW4, V7	GCOWQPVC# (542)
Contryphan-Ar-1	ZYGCOOGLWCH^ (543)
C. arenatus contryphan 1A	ASGCPWRPWC# (544)
C. arenatus contryphan 2	ZYGCPVGLWCD^ (545)
C. arenatus contryphan 4	SGCPWQPWC# (546)
C. arenatus contryphan 1	SGCPWHPWC# (547)

* P may be Pro or hydroxy-Pro; Z may be Gln or pyro-Glu.

TABLE 7

Alignment of α A-Conopeptides* (SEQ ID NO:)

α A-EIVB	GCCGKYONAACHOCGCTVGROOYCDROSGG# (548)
P4.1	GCCGSYPNAACHPCGCK-DRPSYCGQ# (549)
30 P4.2	EGCC---SNPACHPCGCK-DRPSYCGQ# (550)

* P may be Pro or hydroxy-Pro

TABLE 8

Alignment of Bromosleeper Conopeptides* (SEQ ID NO:)

Bromosleeper-Ar1	VVTEACEESCEEEKHCCHVNNGVPSCAVICW# (551)
Bromosleeper-Ar1A	IVTEACEESCEDEEKHCCHVNNGVPSCAVICW# (552)
Bromosleeper-Ar2	IVTEACEEHCEDEEQFCCGLENGQPFCAVCF# (553)
Bromosleeper-Ar3	VVTGACEEHCEDEEKHCCHVNNGVPSCAVICW# (554)
40 Bromosleeper-Di1	NVDQECIDACQLEDKNCCGRTDGEPRCAKICL# (555)
Bromosleeper-Di2	ETDQECIDICKQEDKKCCGRSNGEPTCAKICL# (556)
Bromosleeper-Di3	ETDQECIDTCEQEDKKCCGRTNGEPVCAKICF# (557)
Bromosleeper-P1	PKTEACEEVCELEEKHCCCIRSDGPKCSRKCLLSIFC^ (558)
Bromosleeper-P2	VVSEECKKYCKQKNKCCSSKHEEPRCAKICF# (559)
45 Bromosleeper-Sn	AVTEACTEDCKTQDKCCGEMNGQHTCAKICL# (560)

Bromosleeper-T1 PKTKECERYCELEEKHCCCIRSNPKCSRICIFKFWC^ (561)
 Bromosleeper-T2 PKTRECEMQCEQEEKHCCRVDRGTGQCAPKCLGINW^ (562)

* The E may be Glu or Gla, the P may be Pro or hydroxy-Pro, and W may be Trp or bromo-Trp.

TABLE 9

Alignment of Conopressins (SEQ ID NO:)

Conopressin-G CFIRNCPKG# (563)
 10 Conopressin-S CIIRNCPRG# (564)

TABLE 10

Alignment of O-Superfamily (SEQ ID NO:)

Ar6.1 -----GCTPPGGVCGYHGH---CCD-F-C---DTFGNLCVS# (565)
 5 C. geogr. GS-A -----ACSGRGSRCPPQ-----CCMGLTC--GREYPPRC# (566)
 Ca6.3 (F166) -----NCGEQGEGCAT--RP--CCSGLSC-VGSRPGGLCQY# (567)
 convulsion -----NCPY-----CVVY-----CCPPAYCEASG-----CRPP# (568)
 De6.1 -----ACKOKNNLCAITXMAX--CCSGF-CLiy-----RC^ (569)
 Lv6.2 (I16) -----SCGHSAGACYT--RP--CCPGLHC-SGGQAGGLCV^ (570)
 20 Lv6.3 (I12) -----DCGESGQGCYSV-RP--CCPGLICKGTG-GGGLCRPSGI^ (571)
 Mf6.1 (F204) -----CTPPGGLC-YHAYP--CCSKT-C---NLDTSQCEPRWS^ (572)
 Mi6.2 (F162) -----CTDDSQFCNPSNHD--CCSG-KCIDEQDNG-ICAIVPENS^ (573)
 Mi6.3 (F161) -----CTEDSQFCNPSNHD--CCSG-KCIDEQDNG-ICAIVPENS^ (574)
 Pu6.1 (JG14) -----CSDFGSDCVPATHN--CCSG-ECFGFEDFG-LCT^ (575)
 5 Qc6.4 (F025) -----ACSQVGEACFPQ-KP--CCPGFLC--NH-IGGMCHH^ (576)
 S6.4 -----CLPDGTSCLF SRIR--CCGT--C---SSILKSCVS^ (577)
 Ts6.3 (F081) -----SCAEFGVC-SS-TA--CCPDLDCEAYSP--ICLWE^ (578)
 Tx6.3 -----KCVEQWKYCTR---ESLCCAGL-CLFS-----FCIL^ (579)
 Tx6.7 -----CVEQWEVCGIILFSSSCCGQL-CLFG-----FCVL^ (580)
 30 Vr6.1 (F198) -----DCGGQGEQCYT--QP--CCPGLRCRGGGTGGGVQCL^ (581)
 Wi6.1 (M406) FGSFIPCARLGEPC-----T-ICCRPLRCRESG--TPTCQV^ (582)
 Rg6.6 (K861) -----TCLEHNKLCWYD---RDCCTIY-C---N--ENKCGVKPQ^ (583)
 EST202 -----ACKSNYDCPQRFKCCSYTWNGSSGYCKRVCYLYR^ (584)
 35

TABLE 11

Alignment of ψ -Conopeptides* (SEQ ID NO:)

ψ -PIIIF GOCCLYGSCROFOGCYNALCCRK# (585)
 40 U021 homolog HPPCCMYGRCCRYPGCSSASCCQG# (586)

* P may be Pro or hydroxy-Pro

TABLE 12

Alignment of kappaA-Conopeptides* (SEQ ID NO:)

45 Cn10.3 (J454) APELVVTTATTTCCGYDPM TICPPCMCTHSCPPKRKP# (587)
 A10.2 (H350) ZSWLV PSTITTTCCGYDPM TCPPCRNNTCKPKKPKPGK# (588)

Cn10.4 (G851)	APELVVTATTTCCGYDPMTWCPSCMCTYSCPHQRKKP# (589)
M10.3 (X003)	APELVVTATTTCCGYDPMTCPPCMCTHSCPPKGGP# (590)
A10.3 (AA400)	ZKWLHVHISKITYCCGYNKMDMCPPCMCTYSCPPLKKKRP# (591)
A10.4 (AA401)	APWTVVTATTNCCGITGPG-CLPCRCTQTC# (592)

5

TABLE 13Alignment of α -Conopeptides (SEQ ID NO:)

10	G1.4	-ECCHPACGKHYSC# (593)
	G1.5	-ECCNPACGRHFSC# (594)
	S1.8	AYCCHPACGPNYSCGTSCSRTL^ (595)
	S1.9	AYCCHPVCGKNFDC# (596)
	Ra1.1	GCCCNPACGPNYCGTSCSRTL^ (597)
15	Ar1.1	ZDYCCTIPSCWDYKERCRRHIR^ (598)
	Er1.1	ZDYCCTIPSCWDYKERCRRHIR^ (599)
	Mil.2	-DYCCHRGPCMVMW----C# (600)
	Jp1.1	--GCCSDPRC--RYR--CR^ (601)
	a-OmIA	--GCCSHPACNVNNPHICG# (602)
	a-OmIA [COOH]	--GCCSHPACNVNNPHICG^ (603)
20	Qc1.1	Z-GCCSDPACAVSNPDICGG# (604)
	Bn1.6	PE-CCTHPACHVSHPELC# (605)
	Mr1.5	PE-CCTHPACHVSNPELC# (606)
	Mil.1	---CCNHPACAGKNSDLC# (607)
	MII[YHT]	--GCCYHPTCHLEHSNLC# (608)
25	Nb1.1	--GCCERPPCRWQNPDLG# (609)
	Ak1.1	--TCCSRPTCRMEYPELCG# (610)
	Qc1.2	NE-CCDNPPCKSSNPDLCDWRS^ (611)
	Lp1.1	---CCSNPACNRYNPAICD^ (612)
	Em1.1	-D-CCNFPAASNPGLCT^ (613)
30	C. victor alpha	---CCSSPPCFASNPA-C# (614)
	Cj1.1	-GGCCSFPPCIANNPF-CA# (615)
	Fd1.1	--GCCSNPPCSYLNPA-C# (616)
	Em1.2	-D-CCSDPPCAHNNPD-CR^ (617)
	Gel.1	--GCCSNPPCYANNQAYCN# (618)
35	Wil.1	DE-CCAHPSCWKAEDLICTNQRRRTL^ (619)
	Cal.5	--GCCAIRECRLQNAAYCGGIS^ (620)
	Bt1.10	SATCCYYPPCYEAYPESCL^ (621)

TABLE 14

Alignment of Conopeptides* (SEQ ID NO:)

40	Convulsant	VYXTHP^ (622)
	WG002	WSWRMGNGDRSDQ^ (623)
45	QcII	DCQPCGHNVC^ (624)
	Scratching, Convulsion	KFLSGGFKXIVCHRYCAKGIAKEFCNCPD# (625)
50	MAG-1	RPKNSW^ (626)

MAG-2	AROKNSW? (627)
MAG-3	ROKNSW^ (628)
EST66	CCPSSKEDSLNCIETMATTATCMKSNKGEIYSYACGYCGKKKESCFG DKKPVTDYQCQTRNIPNPGGAAL^ (629)
G12.2	DESKCDRCNCAELRSSRCTQAIIFCLTPELCTPSISCPTGECRCCTKFH QSRCTRFVECVPNKCRDA^ (630)
G12.1	DDSYCDGCLCTILKKETCTSTMSCRG- CRKEWPCWEEDCYCTEIQG GACVTPSECKPGEC^ (631)
EST171	GCVYEGIEYSVGETYQADCNTCRCDFDLATCTVAGCTGFGPE^ (632)
U010 homolog	SGPADCCRMKECCTDRVNECLQRYSGREDKFVSFCYQEATVTCGSFN EIVGCCYGYQCMIRVVKPNSLSGAHEACKTVSCGNPCA^ (633)
P29	DCCGVKLEMCHPCLCDNSCKNYGK# (634)
EST87	GAPIPTTVINYGECKDPSCWVKVKDFQCPGASPPN^ (635)
Ge3.1 (F590)	QCCTFCNFGCQPCCVP^ (636)
Ts10.1	DGCPPHPVPGMHKCMCTNTC (637)
Conophysin-R	HPTKPCMYCSFGQCVPGHICCGPTGCEMGTAEANMCSEEDDPIPCQV FGSDCALNPNPDNIHGHCVADGICCVDDTCTTHLGCL^ (638)

* Conopeptides grouped together are homologous.

[0080] It will be appreciated that the methods and compositions of the instant invention can be incorporated in the form of a variety of embodiments, only a few of which are disclosed herein. It will be apparent to the artisan that other embodiments exist and do not depart from the spirit of the invention. Thus, the described embodiments are illustrative and should not be construed as restrictive.

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